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COVER: This interesting photograph of equipment used by pharmacists in Colonial days was taken in the Hugh Mercer Apothecary Shop, Fredericksburg, Va. Mercer served as Apothecary General in the Revolutionary Army, and his shop was frequented by patriots such as George Washington. The "Friends of Historical Pharmacy" maintain the old shop as a pharmaceutical shrine. Located 54 miles from Washington, D. C., it is now open daily to tourists, after having been closed for some months due to a lack of caretakers.

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NO VA ADVERTISING

THE announcement that 42 states and the District of Columbia now furnish prescriptions to war-disabled veterans under the Veterans Administration plan makes it clear that pharmacy will cooperate nationally to provide this needed service. That the government's obligation can be fulfilled through private practitioners is certainly of advantage. It also carries responsibilities.

One such responsibility, leading to some misunderstanding and abuse, is the iron-clad requirement that VA service must not be advertised to the public. To avoid misunderstandings, this point has been well emphasized in VA agreements and communications. Some pressure to change the ruling and instances of violations have nevertheless arisen. Any form of advertising can be expected to lead to cancellation of the pharmacist's participation agreement.

It has been a timeless tradition of the medical profession not to advertise professional services. Although this custom does not prevail in pharmacy, the VA medical department naturally finds it difficult to see why a professional service, such as pharmacists offer, requires promotion.

Aside from this view, Federal policy does not permit the use of United States government prestige in promoting a private enterprise. Identifying such service with the government implies government inspection, control and approval. At least so officials believe.

Sometimes it is best to leave well enough alone.

A logical objection may be raised, however: Not knowing which pharmacies may fill a VA-authorized prescription inconveniences the veteran. To avoid this, lists of participating pharmacies in each area will be supplied to physicians authorized to prescribe. Pharmacists, individually and as local organizations, also may rightfully place the names of participating pharmacies before their physicians. When there has been adequate lay publicity concerning state association members supplying VA service, a decal on the front of the pharmacy indicating association membership will be helpful.

If it still appears that the veteran is seriously inconvenienced, it might be well for the Veterans Administration to resurrect the now-shelved proposal that a decal be authorized directly identifying sources of VA prescription service. We believe even government policy could justify this move, since it parallels the policy of identifying culture stations by boards of health. Meanwhile, we shall do well to abide by ethical tradition and the government's ruling on advertising.

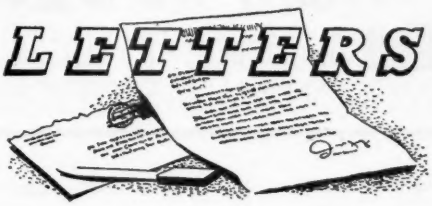
CHANGE FOR THE BETTER

SOME time ago the Civil Service Commission announced that it had changed its mind. Just how much it had changed was indicated in the *Federal Register* last month. Said Commission President Mitchell: Government pharmacists may hereafter advance to the professional grade P4. Applicants must be licensed pharmacists holding a B.Sc. in pharmacy, or an equivalent degree.

Thus the door opens to development of pharmacy's service and status throughout government comparable to that achieved recently in the Veterans Administration. This is progress in seven-league boots considering the Commission's stand as late as last year. No formal professional training was then deemed necessary. It was a stand which precipitated the prolonged controversy between the Commission and the AMERICAN PHARMACEUTICAL ASSOCIATION.

Minimum educational standards had kept salaries at a minimum for too long—at a level that could not possibly provide incentive for many high caliber men capable of providing the kind of pharmaceutical service needed. Not that many incumbent pharmacists, lacking present-day education, fail to serve capably. But with standards so low, and Civil Service procedures being what they are, there was little assurance that an agency would get the able men instead of those who had closed the door on new knowledge or were largely interested in getting on a list for retirement with pay.

Once modern educational requirements were adopted, it is natural that the newly defined policy should reveal increased opportunities for advanced professional ratings with salaries ranging from $2644 up to $5905 annually. On this basis Civil Service may expect to attract many more qualified pharmacists who can demonstrate—in places that count—the modern, progressive role of pharmacy in medical care. The Civil Service Commission has acted wisely, however regrettable the fact that building sound standards for future pharmaceutical service requires breaking with the past.



CREDIT TO THE JOURNAL AND THE GUINEA PIG

Sirs:

I have just read the series of articles on animal experimentation in the September issue of the *Practical Pharmacy Edition* of the JOURNAL. . . . Pharmacists are in a position, even more so than physicians, to play a major role in straightening out public thinking on this subject. I believe that these articles will go a long way toward enabling pharmacists to do this important missionary work.

Medical College of Virginia — H. B. HAAG, M.D.
Richmond, Va.

BACK HOME TO PHARMACY

Sirs:

I am now out of the Service and back home. Your diligence in seeing that I received my JOURNALS overseas has been deeply appreciated. . . .

Sincere congratulations on the excellent job A. PH. A. is doing and has done. I hope I'll soon be doing what I can to further the interests of professional pharmacy.

Buffalo, N. Y. — RICHARD R. SHERWOOD

HE LIKES US

Sirs:

. . . I am finding the *Practical Pharmacy Edition* by long odds the most for my money of any professional reading I receive, and wish I might have had it years ago. With thanks,

Dresden, Ontario — E. HUGH WATSON

BOOKS ON BIOLOGICALS

Sirs:

Who publishes a good book on antitoxins, vaccines and other biologicals? . . .

Gulfport, Miss. — JONES BROS. DRUG. CO.

For pharmacists, Dr. Louis Gershenfeld's book on Bacteriology and Allied Subjects *is one of the best for this purpose. It is available from the Mack Publishing Co., Easton, Pa. The A. M. A.'s* New and Nonofficial Remedies, *which we consider a "must" for the reference shelf, includes an informative chapter on serums and vaccines.*—THE EDITOR

THE READER'S VIEWPOINT

Sirs:

I have read the editorial on "Penicillin Problems" [July], and it seems to me that pharmacists should realize the necessity of restricting this important drug to prescriptions without the necessity of legislation. However, there are two sides to the matter. I think a great many pharmacists resent the fact that drugs such as penicillin troches are restricted items, when their manufacture fails to comply with state laws. . . .

As we know, a number of manufacturers do not have registered pharmacists to supervise "compounding" as required by most state laws. . . . Personally I am of the opinion that drugs should be restricted to drug stores and dangerous drugs to prescriptions, but I am equally interested in knowing that manufacturers are complying with the law by having registered pharmacists in charge of all compounding during manufacture. I believe the AMERICAN PHARMACEUTICAL ASSOCIATION could render a service to the people of the United States by making this an objective.

Chicago, Ill. — J. L. CRAWFORD

DENTAL AND COSMETIC FORMULAS

Sirs:

Have you any books containing formulas of dental and cosmetic preparations which are available to me?

Irvington, N. J. — H. J. GERBER

Pharmaceutical Recipe Book III, *an A. Ph. A. publication, includes special sections on cosmetic and dental formulas. Price: $5; to active members, $3.50. One of the most comprehensive books in the cosmetic field is De Navarre's* The Chemistry and Manufacture of Cosmetics (*D. Van Nostrand Co., New York, $8*). *We believe you would also be interested in* Accepted Dental Remedies (*American Dental Association, Chicago, $1.50*). *This volume contains a small section on dental formulas, but also includes much valuable information for the pharmacist interested in developing a more effective relationship with the dental profession.*—THE EDITOR

FROM A NEW MEMBER

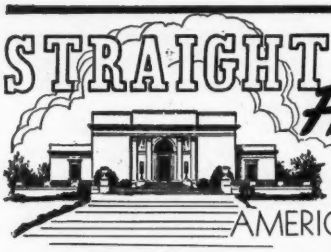
Sirs:

Thank you for your cordial invitation to join in the membership of the ASSOCIATION. I am enclosing $7 which, I believe, takes care of the dues, etc. If not, please advise me.

Your last article on "Ophthalmic Solutions" is worth more than the money I am herewith forwarding.

Alexandria, La. — R. J. BIENVENU

This department is your pharmacy forum. Do you have something to say on current affairs in the profession. . . a question to be discussed? Write to the JOURNAL at 2115 Constitution Ave., N. W. Washington 7, D. C.



STRAIGHT FROM HEADQUARTERS

by ROBERT P. FISCHELIS, Secretary
AMERICAN PHARMACEUTICAL ASSOCIATION

NEW FUNDAMENTAL PRINCIPLES

HOW far reaching health and medical care become in their national and international significance can best be grasped by stating the principles which the 61 nations constituting the World Health Organization adopted as "basic to the happiness, harmonious relations and security of all peoples." Here they are:

"Health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.

"The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social conditions.

"The health of all peoples is fundamental to the attainment of peace and security and is dependent upon the fullest cooperation of individuals and States.

"The achievement of any State in the promotion and protection of health is of value to all.

"Unequal development in different countries in the promotion of health and control of disease, especially communicable disease, is a common danger.

"Healthy development of the child is of basic importance; the ability to live harmoniously in a changing total environment is essential to such development.

"The extension to all peoples of the benefits of medical, psychological, and related knowledge is essential to the fullest attainment of health.

"Informed opinion and active cooperation on the part of the public are of the utmost importance in the improvement of the health of the people.

"Governments have a responsibility for the health of their peoples which can be fulfilled only by the provision of adequate health and social measures."

The United States of America was not only one of the participants in the Conference which formulated these principles, but Surgeon General Parran of the U. S. Public Health Service was the permanent chairman of the Conference. Such international organizations set the tempo for national, state and local activity, and groups like the Allied Health Council of Alabama, the Conference of Allied Medical Professions of New Jersey and other similar groups will undoubtedly share in the planning and execution of measures calculated to translate the phraseology of the principles of good health and good medical care into the necessary action at the grass roots, so that lip service so freely given to proposals for the public welfare may be converted into evidence of healthier communities and happier individuals.

Fortunate indeed are the citizens of states in which the professional groups which are concerned with medical care have organized themselves into harmonious working bodies, capable of examining cooperatively the problems which confront all and taking counsel of one another as to the best methods of realizing the full benefit of the contribution which each group can make to the problem as a whole.

As pharmacists, we can take considerable pride in the knowledge that pharmaceutical associations have contributed so largely to the organization of groups engaged in supplying health and medical care services in various states.

Pharmacists are in the vanguard of the army of workers in the field of public health. Their establishments, strategically located throughout the length and breadth of this land, are the outposts for public health education. Alert and able health officers are aware of this fact and have taken full advantage of the possibility for spreading public health information to remote sections through pharmacies. We must not fail them.

STANDARDS MUST BE MAINTAINED

Our expanded educational program, our high standards of licensure, the continual effort of our colleges of pharmacy to provide refresher education, and the activity of national and state pharmaceutical associations to keep their members posted through their professional journals are evidence of the seriousness with which phar-

macists approach their growing contribution to health and medical care.

It would be nothing less than tragic for any state to now take a step backward by entertaining any proposition to lower its standards under the guise of meeting a temporary shortage of pharmacists somewhere. We struggled through the war years without sacrificing standards. Why let down the bars now when our colleges of pharmacy are filled to overflowing with earnest and eager men who have returned from the battle fronts? These men should be given every opportunity to come into the profession without being required to compete against those who have failed to meet standards which are today regarded as minimum for the character of work that needs to be performed. Returned veterans now pursuing pharmacy courses should make themselves heard in every state where lowering of Standards of registration is proposed. A move to lower standards of registration is a move to impair pharmaceutical service to the public.

Boards of pharmacy, pharmaceutical associations, pharmacy college faculties and student bodies must stand watch over our present laws to see that they are not tampered with except to bring standards up to minimum levels where that is necessary.

THE DRUG TRADE CONFERENCE

The National Drug Trade Conference gained its early reputation by bringing the various branches of the drug industry together in support of federal narcotic legislation at the time the Harrison anti-narcotic law was before Congress, about 1914. The Conference supported this legislation. By its "unanimous action" rule it has failed to take a stand on many very important problems affecting pharmacy. This rule provides that if any member of the Conference (three delegates from each of three national manufacturing and two national wholesale associations, the N. A. R. D., the A. PH. A., the Association of Colleges and the Association of Boards of Pharmacy) chooses to declare a proposal controversial, no action can be taken on it by the Conference.

Hardly another important action was taken until a uniform State Food, Drug and Cosmetic bill was agreed upon. Next, unanimous action was forthcoming when the American Foundation for Pharmaceutical Education was organized. This year the Conference faces another important test. For years the A. PH. A. and the N. A. R. D. together with the associations of colleges and boards of pharmacy have advocated the restriction of the sale of drugs and medicines to establishments operated and supervised by pharmacists. The Proprietary Association has been the leading opponent of legislation seeking to accomplish this.

At the last annual meeting of the Conference a Committee on Uniform State Legislation was named, largely for the purpose of determining whether there could be brought about a meeting of minds on all state legislation affecting the profession of pharmacy and the drug industry. This would of course include restrictive legislation covering the sale of drugs and medicines. Just what any group in the drug industry would have to lose by agreeing to have all drug products dispensed in pharmacies under the supervision of trained pharmacists is not apparent. Certainly the public would be benefited by added protection to which it is entitled. The volume of sales would not be decreased. The products would reach the public in a more acceptable form and there would never be any difficulty in tracing the location of a product should anything go wrong in its production, as has happened. Every pharmacy is recorded either officially or unofficially with boards of pharmacy and responsibility for any dereliction in dispensing can be traced and punished. Who is holding back progress in drug distribution under conditions of control which are distinctly in the public interest and for what purpose is such control being denied?

THIRD JOINT MEETING

On November 23 the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION and the Executive Committee of the National Association of Retail Druggists will hold the third annual joint meeting of these two bodies in Chicago. Again they will discuss all of the worth-while resolutions and recommendations emanating from state pharmaceutical associations and other sources. This is a conference which has proven to be very useful for the purpose of exchanging ideas. The joint meeting or conference considers the text and the background of various proposals in order to avoid duplication of effort as well as to assure that no worthy proposal is overlooked. It is a remarkably effective clearing house which provides a forum for discussion at a high administrative level. American pharmacy is fortunate in having this forum available and those participating in this third annual conference are fully aware of their responsibilities.

pH SOME PHARMACEUTICAL APPLICATIONS*

by E. L. CATALINE

UNIVERSITY OF MICHIGAN, COLLEGE OF PHARMACY

THE importance of proper adjustment of the degree of acidity or alkalinity of pharmaceutical preparations becomes increasingly apparent. A relatively few years ago pharmacists seldom, if ever, changed the reaction of a solution or other preparation. It is now becoming much more common, not only in the large-scale manufacture of pharmaceuticals but also at the prescription counter.

Buffered collyria are frequently called for; and there is every reason to believe that, in the future, prescriptions for other types of preparations, such as lotions and ointments, will be found to require adjustment of acidity or alkalinity. Thus, the methods and procedures of such adjustments and the principles underlying them are constantly assuming greater importance for the pharmacist. In the discussion below, a few of the many applications of *p*H are presented to indicate present practices and probable trends.

Meaning of pH

The term *p*H is defined as "the negative logarithm of the concentration of the hydrogen ion." The hydrogen-ion concentration may be expressed in a number of ways most of which are rather cumbersome. For example, it has been found that in pure distilled water there is about seven ten-millionths of a gram of hydrogen ions per liter. This may be expressed as a decimal fraction, 0.0000007 Gm. per L., or exponentially, 1×10^{-7} Gm. per L. However, in practice these forms are not always convenient and a simpler means of expression is certainly desirable.

The term *p*H, suggested by Sörenson,[1] and defined above, has come into very common use because it does have simplicity to recommend it. In the example of the distilled water, it was pointed out that the concentration of hydrogen ions could be stated as 1×10^{-7} Gm. per L. In this expression, it is seen that the logarithm is -7. Thus, the *p*H, being the negative logarithm, would be minus -7, or $+7$. This is obviously a more simple form of expressing the hydrogen-ion concentration than are the decimal fraction or exponential forms.

In a solution which contains 1×10^{-2} Gm. of hydrogen ions per liter, the *p*H is 2, while a solution containing 1×10^{-10} Gm. of hydrogen ions per liter has a *p*H of 10. On this basis there has been constructed a *p*H "scale" from 1 to 14 which is widely used to express conveniently the concentration of hydrogen or hydroxyl ions. A *p*H of 7 represents neutrality. When the *p*H is less than 7 an acid reaction is signified, and an alkaline reaction is indicated by a *p*H above 7.

It is important to understand that although it is commonly said that a solution having a *p*H of 2, for example, is "very strongly acid," and one with a *p*H of 13 is "very strongly alkaline," such solutions are in reality very dilute.

For instance, if one dilutes 1 cc. of hydrochloric acid U. S. P. to 1000 cc. with distilled water, the *p*H of the resulting solution will be about 2 and the percentage concentration will be 0.0365%. If 1 cc. of hydrochloric acid U. S. P. is diluted with distilled water to 1,000,000 cc. the *p*H of the solution produced will be 5, the concentration being 0.0000365%. Thus, it is clear that in this range we are dealing with very dilute solutions. But as will be seen below, small changes, such as from *p*H 7 to *p*H 3, are of decided importance in connection with the stability, therapeutic efficacy and other characteristics of many preparations.

pH and Stability

One of the unfortunate characteristics of many pharmaceutical preparations is their relative instability. Precipitation, loss of activity, change of color, and other changes are often

* Based on an address delivered before the Northwestern Ohio Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION.

characteristic of some preparations and occur at times in others. In many instances it has been found that these evidences of instability are due to the development, in one way or another, of an unfavorable *p*H either during manufacture or subsequently.

In a number of cases it has been found that proper adjustment of the *p*H by adding appropriate substances overcomes the difficulty in part or wholly. A few examples will illustrate this.

Tincture of aconite N. F., prepared by using the usual hydro-alcoholic menstruum, undergoes deterioration rather rapidly, losing its activity to a considerable extent. This loss of activity is associated with the hydrolysis of the alkaloid aconitine. After it was shown that the hydrolysis takes place rapidly in alkaline solution but very slowly in acid solution,[2] Swanson[3,4] found that the addition of a small amount of acid to the menstruum or to the fresh percolate would so stabilize the tincture that its loss of activity was practically negligible. In line with this finding, the N. F. VII directs that hydrochloric acid be added to the percolate until the *p*H is 3 ± 0.2.[5] Tinctures so prepared are exceedingly stable under the usual conditions of storage and use.

In a similar way, it has been shown that the addition of tartaric acid to tincture of digitalis until the *p*H is 5.4 will materially decrease the deterioration commonly seen in this preparation.[6,7] At higher *p*H there is considerable loss of activity and the higher the *p*H, the greater the loss.

Other examples which may be cited include elixir of three bromides N. F. in which the color change that often occurs can be minimized by adjusting the *p*H of the preparation to 4.2,[8] and solutions of thiamine chloride which are most stable when the *p*H lies between 3.5 and 4.5. Not only are solutions of thiamine chloride more resistant to atmospheric oxidative changes in the *p*H range 3.5–4.5, but they may be sterilized at 120° C. for 20 minutes with very little decomposition when so adjusted.

pH and Therapeutic Efficacy

Besides being of assistance in stabilizing preparations, the adjustment of *p*H to the proper value is often followed by increased therapeutic activity. This is particularly true of antiseptics with which some rather remarkable results have been obtained. Several years ago, Degering and his co-workers[9] found that the antiseptic and bactericidal activity of a number of antiseptics was strikingly increased when the *p*H of their solutions was properly adjusted.

In Table I the results obtained with some typical antiseptic substances are shown. It is seen that as the *p*H of solutions of these substances is lowered from 7, little change is apparent until *p*H 4 or 3 is reached. Then there is a remarkable increase in activity.

TABLE I.—BACTERICIDAL ACTION OF ANTISEPTICS

*p*H	Highest Killing Dilution (*Staph. aureus*)
Benzoic Acid	
8	1:5
7	1:10
6	1:10
5	1:20
4	1:250
3.5	1:900
Phenylmercuric Nitrate	
7	1:10,000
6	1:20,000
5	1:10,000
4	1:10,000
3	1:100,000
Hexylresorcinol	
7	1:3,000
6	1:3,000
5	1:5,000
4	1:12,500
3	1:100,000
Merthiolate	
7	1:10,000
6	1:5,000
5	1:10,000
4	1:75,000
3	1:75,000

In some of the instances cited, a change from *p*H 4 to 3 is accompanied by a nearly tenfold increase in activity and the same is true with many other substances. In a few instances—sulfonmerthiolate, for example—the antiseptic activity was greater in alkaline medium (*p*H greater than 7) than in acid medium (*p*H less than 7), but such cases were the exception.

An excellent illustration of the effect of *p*H on antiseptic activity is found in the case of mandelic acid. This urinary antiseptic is not significantly bactericidal in alkaline urine, nor in acid urine when the *p*H is greater than 5.5. When the *p*H is below 5.5 mandelic acid is a very effective bactericide, and in clinical practice the attempt is made to keep the *p*H of the urine below 5.5.[10]

The fact that methenamine liberates formaldehyde, and therefore acts as a urinary antiseptic, only in a strongly acid medium (*p*H below 5.0) is well known. In this instance, as in the case of mandelic acid, it is common practice to administer an acidifying salt such as ammonium chloride or sodium biphosphate to render the urine acid.

Thus far, only a few papers have appeared

which report results of investigations into the possible importance of the *p*H adjustment of lotions and ointments, but they give reason to believe that rather important developments will be forthcoming in the near future.

According to Harry[11] it is quite possible that external preparations are most efficacious when they do not materially interfere with the functions of the "acid mantle" of the skin. Even though these functions are not at all understood at the present time, it is thought that the acid mantle may possess antibacterial activity of some sort which protects the individual against the innumerable microorganisms which normally inhabit the skin.

On this basis, the use of external preparations that possess a *p*H the same as that of the normal skin would seem to be indicated. On the other hand, it is possible that ointments and lotions of definite *p*H, differing from that of the acid mantle, may be of value in restoring the normal *p*H of the skin when pathologic conditions may have altered it from the normal (which ranges from *p*H 4.2 to 5.6, averaging from 5.3 to 5.6). Harry has suggested a number of formulas for creams of definite *p*H that may serve as starting points in the development of this field.*

Buffering

So far the examples mentioned have involved only the addition of a substance such as an acid or alkali until the proper *p*H has been reached. No provision has been made for maintaining the *p*H at the desired point in the event that additional acid or alkali might find its way into the solution. Yet, in many instances it is very desirable that such provision be made. It is possible to prevent the *p*H from changing materially by using what are known as buffer mixtures.

To understand the action of buffer mixtures, it is first necessary to recall the difference between "strong" and "weak" acids and alkalies. By a strong acid or alkali is meant one which, upon being dissolved, undergoes electrolytic dissociation to a considerable extent. In such solutions one finds large concentrations of ions. Examples of strong acids are hydrochloric, sulfuric and nitric which in solution are almost completely dissociated into ions, as indicated by the following equations.

$$HCl \rightleftharpoons H^+ + Cl^-$$
$$H_2SO_4 \rightleftharpoons 2H^+ + SO_4^{--}$$
$$HNO_3 \rightleftharpoons H^+ + NO_3^-$$

When one of these acids is added to distilled water the concentration of hydrogen ions will be greatly increased and the solution will be highly acidic. If, on the other hand, it were possible to immobilize these hydrogen ions in some way the *p*H would not be materially affected. By first dissolving the salt of a weak acid in the water this may be accomplished. Taking sodium acetate as an example of a salt of a weak acid, the reaction upon addition of a strong acid (hydrochloric) would be:

$$NaC_2H_3O_2 + HCl \rightarrow NaCl + HC_2H_3O_2$$

The acetic acid is only very slightly ionized. Thus, most of the hydrogen exists in the form of nearly un-ionized acetic acid and the concentration of hydrogen ions is very low; in other words, addition of the strong hydrochloric acid to the solution of sodium acetate has not materially changed the *p*H.

In the same way, the rise in concentration of hydroxyl ions which would result when a strong base is added may be minimized by having a weak acid present. The reaction in this case would be:

$$HC_2H_3O_2 + NaOH \rightarrow NaC_2H_3O_2 + HOH$$

In this case the hydroxyl ions are combined as water which is, of course, neutral.

If a pair of substances such as acetic acid and sodium acetate are combined in solution they form a buffer mixture. Such a mixture will protect a solution or other preparation in which it may be incorporated against appreciable change in *p*H upon the addition of strong acids or alkalies. A number of such mixtures are available for use by the pharmacist in protecting various types of preparations against changes in *p*H.

Buffered Collyria

Perhaps the greatest progress in buffering extemporaneous pharmaceutical preparations has occurred in the field of ophthalmic solutions. It has been found that much of the irritation resulting from application of solutions to the eye can be eliminated if their *p*H is properly adjusted. In fact, it has been shown that in some instances buffered solutions alone are capable of acting as therapeutic agents.

The best known mixture for buffering collyria is that developed by Gifford and Smith.[12] As a result of their studies, these ophthalmologists found that the following mixtures can be easily

* Mr. Harry's work has been reviewed in THIS JOURNAL, 3, 340, (1942).

employed for the extemporaneous preparation of collyria of rather definite *p*H.

GIFFORD AND SMITH BUFFER MIXTURE

SOLUTION NO. 1

Boric acid, anhydrous	12.4
Potassium chloride, anhydrous	7.4
Distilled water	1000

SOLUTION NO. 2

Sodium Carbonate, anhydrous	21.2
Distilled water	1000

The quantities of each solution required for the preparation of 1000 cc. of a buffer mixture of definite *p*H are shown in Table II.

TABLE II.—GIFFORD AND SMITH BUFFER MIXTURES

*p*H	cc. No. 1	cc. No. 2
5	0	1000
6	1.7	998.3
6.2	3.3	996.7
6.75	8.3	991.7
7.2	33.3	966.7
7.6	50	950
7.8	66.7	933.3
8.2	100	900
8.4	133.3	866.7
9.2	266.7	733.3

Since the normal secretions of the eye have a *p*H which averages about 7.2, it would seem best to adjust the *p*H of ophthalmic solutions to this value. However, for at least two reasons it is not always feasible to buffer such solutions to the same *p*H as that of the eye secretions.

First, the inherent characteristics of the medication employed may make it impossible to buffer to *p*H 7.2. For example, if a solution of zinc chloride is buffered to *p*H 7.2, zinc hydroxide precipitates. Likewise, most alkaloids are soluble in acid solution but are insoluble in alkaline solution. Therefore, these substances, and many others, must be dispensed in solutions whose *p*H is materially different from that of the lachrymal fluid.

Secondly, as pointed out above, the therapeutic efficacy of many substances is optimal at definite *p*H values and these are often considerably different from 7.2. Recognizing these facts, Gifford and Smith determined the optimum *p*H for a number of substances, as shown in Table III.

In addition, Gifford and Smith found that the alkaline buffer mixture of *p*H 9 is useful in the treatment of vernal conjunctivitis and certain cases of chronic conjunctivitis. Moreover, it has been shown that there are other important specific effects of *p*H.[13] For example, solutions which are to be employed in the treatment of pneumococcic and gonococcic infections of the eye are most efficacious when their *p*H is less than 7, while streptococcic infections are more sensitive to solutions having a *p*H greater than 7.

TABLE III.—OPTIMUM pH FOR THERAPEUTIC EFFICACY

MEDICAMENTS	*p*H
Butyn and Phenacaine	5
Zinc salts, epinephrine, cocaine	6
Atropine, physostigmine, pilocarpine, homatropine	7.6
Soluble fluorescein	9

A further use of the Gifford and Smith buffers has been found in connection with the so-called "contact lenses." Before application to the eye these lenses must be filled with liquid. Excellent results have been obtained by employing the proper buffer mixture for this purpose, irritation being reduced to a minimum. No one mixture can be said to be optimal since the eyes of different persons differ in their response. It is necessary to determine by trial, which mixture of definite *p*H is the most satisfactory in each case.

In a recent publication, Arrigoni and Tozer[14] have described the use of mixtures of monobasic potassium phosphate (KH_2PO_4) and dibasic sodium phosphate (Na_2HPO_4) or of sodium acetate and boric acid in the preparation of a number of buffered, isotonic and preserved collyria which give promise of being extremely useful to the practicing pharmacist.

Buffered Collunaria

Solutions which are to be instilled into the nose also should possess a *p*H near that of the nasal secretions, namely 7.2. The nose, however, does not appear to be so sensitive as the eye to slight variations in *p*H. Tozer and Arrigoni[15] found that preparations which varied from *p*H 6.0 to 7.6 were well borne and produced minimum irritation. In their experiments, mixtures of monobasic potassium phosphate and dibasic sodium phosphate were used as buffers.

The importance of the adjustment of *p*H in solutions to be used nasally is emphasized by the work of Fabricant,[16] who has shown that solu-

tions which are slightly acid are more effective in the treatment of colds and sinus infections.

Buffered Ointments

Mention has been made previously of the possible importance of the adjustment of the *p*H of lotions and ointments. While this field has not been extensively developed, there is reason to believe that important advances will soon be seen. Harry[11] has speculated on the desirability of buffering ointments and has published a number of formulas for buffered ointments, utilizing mixtures of solutions of sodium phosphate and citric acid. LeMar and White[17] have shown that "certain buffered ointments tested exhibited greater germicidal action than unbuffered ointments of similar hydrogen-ion concentration."

In studies on the adjustment of non-aqueous systems, however, care must be taken in expressing *p*H meter readings as *p*H. Due to a number of factors, readings may vary considerably from a true representation of the hydrogen-ion concentration.

In a brief discussion of this sort, it is patently impossible to consider all of the applications of *p*H. However, some others might be mentioned to indicate the range of possibilities.

Studies have shown that the stability of emulsions depends in no small measure upon the apparent *p*H of the preparation. This is due to the fact that the charge on the near-colloidal droplets of the emulsions may be altered if the *p*H differs materially from the optimum value. It has been found, for instance, that oil-in-water emulsions promoted by acacia are most stable when the *p*H lies in the range 4.1–4.3 while tragacanth-promoted emulsions are most stable at a pH of about 2.5.[18]

By means of a very efficient buffer system the *p*H of the blood is maintained at 7.35. Whenever it is feasible, solutions which are to be injected intravenously are buffered to about *p*H 7.35 since the injection of such a solution puts relatively little strain on the buffer system of the blood. It should be pointed out, however, that except when large amounts of intravenous solutions are injected, the blood's buffers can usually take care of the acid or alkali contained in injections.

The sterilization of a number of substances in solution is accompanied by considerable breakdown unless the solutions are properly buffered to the appropriate *p*H value. For example, cocaine hydrochloride solutions must be adjusted to *p*H 5 or less, if excessive hydrolysis is to be avoided when the solution is subjected to the heat necessary for sterilization.

When it is necessary to adjust the *p*H of a prescription by the simple addition of acid or alkali, the following method, described by Wyss,[19] may be conveniently used.

Practical Adjustment of pH

"*STEP I.* The prescription ingredients are combined and the preparation is brought to within one-half to one fluid ounce of the desired volume. Using an indicator paper of wide *p*H range,* the approximate *p*H value of the mixture is determined by moistening the paper with a drop of the preparation and comparing the resulting color with the standards provided. This step serves to indicate whether acid or alkali will be needed for the adjustment and to show approximately how far the *p*H of the mixture is from the desired range.

"*STEP II.* Small pieces of indicator paper, especially suitable for showing differences of *p*H over a narrow range of *p*H,† then are placed on a pill tile or other convenient surface. Let it be assumed, for example, that the desired *p*H is to be approximately 4, with an upper limit of 5 and a lower limit of 3. A drop of each of three standard buffer solutions is placed on individual pieces of the indicator paper—one buffer solution representing the upper limit of the desired *p*H range (*p*H 5), one the lower limit (*p*H 3), and one the median value (*p*H 4). The colors thus produced will serve as guides in adjusting the *p*H of the finished prescription.

"*STEP III.* Dilute hydrochloric acid or sodium hydroxide of known strength is added in measured small amounts to exactly 10 cc. of the prescribed mixture as the case requires. Each addition is followed by thorough mixing and testing on fresh portions of indicator paper until the color obtained shows the *p*H of the sample to compare favorably with that produced by the specified standard buffer solution (*p*H 4). From the amount of acid (or alkali) required for the 10-cc. portion of the prescribed mixture, the volume needed for the remainder of the prescription may be calculated.

"*STEP IV.* The calculated volume of acid (or alkali) is combined with the rest of the mixture, the above portion which was subjected to the preliminary adjustment is added, and sufficient vehicle is used to yield the final volume. The completed preparation is mixed thoroughly and subjected to a final check of the *p*H value;

* A number of such papers are now available. Examples are the "pHydrion" paper (Central Scientific Co., Chicago) and "Alkacid Test Ribbon" (Fisher Scientific Co., Pittsburgh, Pa.).—THE EDITOR

† Available from such firms as Precision Laboratories, Rossmoyne, O.—THE EDITOR

if satisfactory, the product is packaged properly and labeled, with complete instructions to the patient concerning proper conditions of storage and use."

REFERENCES

1. Sörensen, S. P. L., *Biochem. Zeit.*, **21**, 131, 201 (1909).
2. Dunstan, W. R., and Carr, F. H., *J. Chem. Soc.*, **65**, 290 (1894).
3. Swanson, E. E., and Walters, A. L., THIS JOURNAL, *Scien. Ed.*, **12**, 957 (1923).
4. Swanson, E. E., *ibid.*, **13**, 1108 (1924).
5. "The National Formulary," Seventh Revision, AMERICAN PHARMACEUTICAL ASSOC., Washington, 1942, p. 440.
6. Joachimoglu, G., and Bose, P., *Arch. exptl. Path. Pharmakol.*, **102**, 17 (1924); through *Chem. Abstracts*, **18**, 2787 (1924).
7. Mascarenhas, cited from *Gaz. Pharmacia*, in *Am. Profess. Pharmacist*, **4**, No. 10, 34 (1938).
8. Guth, E. P., *Bull. Natl. Formulary Comm.*, **11**, 224 (1943).
9. Degering, Ed. F., *et al.*, *Ind. Eng. Chem.*, **30**, 646 (1938); **31**, 742 (1939); **32**, 996 (1940).
10. Goodman, L. S., and Gilman, A., "The Pharmacological Basis of Therapeutics," Macmillan, 1941, p. 840.
11. Harry, R. G., *Brit. J. Dermatol. Syphilis*, **54**, 1 (1942).
12. Gifford and Smith, *Arch. Ophthalmol.*, Feb., 1933; Jan., 1935.
13. Holland, M. O., *Am. Profess. Pharmacist*, **4**, No. 7, 15 (1938).
14. Arrigoni, L., and Tozer, G. A., THIS JOURNAL, *Pract. Pharm. Ed.*, **7**, 292 (1946).
15. Tozer, G. A., and Arrigoni, L., THIS JOURNAL, *Scien. Ed.*, **30**, 189 (1941).
16. Fabricant, N. D., *Arch. Otolaryngol.*, **34**, 150, 302 (1941).
17. LeMar, L. E., and White, A. I., THIS JOURNAL, *Scien. Ed.*, **33**, 134 (1944).
18. Goldner, K. J., in "American Pharmacy," J. B. Lippincott, Philadelphia, 1945, p. 131.
19. (*a*) Wyss, A. P., THIS JOURNAL, *Pract. Pharm. Ed.*, **6**, 6 (1945).
(*b*) Wyss, A. P., *Merck Rept.*, **54**, 16 (1945).

USE OF SYRINGE TO MEASURE TYROTHRICIN

by WILLIAM P. O'BRIEN

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USE of a hypodermic syringe for measuring both small and large quantities of tyrothricin concentrate in making up solutions is ideal for several reasons. It simplifies the production of sterile solutions of this antibiotic, is economical, and permits a high degree of accuracy.

A hypodermic syringe of any size can be used. However, for very small quantities, a 1, 1.5 or 2 cc. syringe is most suitable.

For topical applications or for instillation into one of the body cavities, the pharmacist can easily prepare sterile solutions within a reasonable time. As an illustration, the preparation of a liter of tyrothricin solution may be described as follows.

Materials and apparatus necessary:

1—20-cc. package of tyrothricin concentrate, 2.5%.
1—1000-cc. rubber-capped flask of sterile distilled water.
1—20-cc. syringe with a small gauge hypodermic needle.

Procedure—Sterilize the syringe and needle by boiling in a 1% phenol solution for thirty minutes or by autoclaving. Attach the needle to the syringe with the aid of forceps or tweezers and push the piston all the way in, to drive out any water.

Wipe off the rubber caps of the tyrothricin vial and distilled water flask with 70% alcohol or antiseptic solution before inserting the needle. Insert needle into the cap of distilled water flask and withdraw 20 cc. of water. This is discarded after the syringe is withdrawn. Then insert needle into the cap of the tyrothricin vial and withdraw 20 cc. Remove needle and insert into distilled water flask and empty contents into the water. Before withdrawing needle invert flask and draw 15 to 20 cc. of the solution into syringe and return to flask by emptying the syringe, thus rinsing out residual tyrothricin. Shake the flask of solution to mix thoroughly.

Often the pharmacist is called upon to prepare solutions that require very small quantities of tyrothricin. Such solutions are frequently prescribed by eye and ear specialists and call for only 0.15 to 0.3 cc. of tyrothricin concentrate, 2.5%. The following prescription is a familiar example.

℞

Sol. Tyrothricin 200 micrograms per cc.
Disp. 15 cc.

To fill the above prescription 0.12 cc. of tyrothricin concentrate is needed. This amount can be measured rather accurately with a 1 cc. B-D Yale syringe graduated in 0.1 cc. (The 0.02 cc. is approximated as closely as possible.) The syringe should be rinsed in the finished solution by drawing in and expelling some of the solution several times. In this manner all the tyrothricin measured is used.

The hypodermic syringe permits greater accuracy of measurement than graduates permit. Also, by use of the hypodermic syringe, the tyrothricin can be withdrawn from a 10- or 20-cc. stock vial without any waste and then added to the measured water in a sterile container. When a hypodermic syringe is employed, the tyrothricin always will be added to the water, and thus the mistake of adding the water to the tyrothricin cannot be made. To produce a clear solution the tyrothricin concentrate must be added to the water.

PROTEIN .IN MODERN THERAPY

by L. EARLE ARNOW*

INDICATIONS FOR PROTEIN DIETARY SUPPLEMENTS ARE VIEWED IN THEIR RELATION TO METABOLIC FUNCTION . . . NATIVE PROTEIN SUITABLE IN MOST CASES, WHILE AMINO ACID MIXTURES SUPPLY NEED FOR SOLUBLE FORMS

ALL living cells are dependent for their very existence on proteins. The average human body is about 66% water and is almost 20% protein. If we exclude the water, this means that about 56% of the dry weight of the body is protein.

Such familiar things as hair, skin, eye coloring, wool, silk and leather owe their distinctive properties to the proteins present in them. Even the color in the cheeks of a blushing maiden (assuming one can be found these days) is due to hemoglobin, the red protein of the blood that carries oxygen to the tissues.

Protein molecules are huge as compared with other common organic molecules. It may be recalled that the molecular weight of water is approximately 18; of ordinary cane sugar, about 300; and of an average fat molecule, about 1000. In contrast to this, the molecular weights of proteins range from about 3000 to something in the neighborhood of 50,000,000.

It is not surprising, therefore, that the detailed structure of protein molecules is not known with certainty. We do know, however, that each of these huge molecules can be broken down by relatively simple procedures into a mixture of smaller organic molecules known as amino acids. The name "amino acid" indicates that these simpler compounds contain both acid (COOH) and amino (NH_2) groups. Much study has convinced us that protein molecules are formed when a number of these amino acids combine chemically together with the elimination of water. When this water is added chemically to the protein molecule, as occurs, for example, during digestion, the amino acids are formed again.

Most of the common proteins contain 20 to 22 different kinds of amino acids chemically combined together. In most cases several amino acids of one kind will be present at different locations in the protein structure. One of the proteins circulating in blood plasma, for example, probably contains between 300 and 400 of these amino acid molecules in each protein molecule.

All of these amino acids contain carbon, hydrogen, oxygen and nitrogen. Some of them contain sulfur, and some of them are combined with phosphoric acid when they are present in proteins. Since in contrast to other common substances, such as sugars and fats, all proteins contain nitrogen, it is customary to estimate the content of protein in a tissue or medicinal preparation by determining the amount of nitrogen present. If the amount of nitrogen as determined by chemical analysis is multiplied by the factor 6.25, the resulting figure is a fairly accurate measure of the amount of protein present. It will be noted that this calculation involves the assumption that proteins contain about 16% nitrogen.

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Essential Amino Acids

In extensive experiments involving the use of laboratory animals, it has been found that the animal body can synthesize or manufacture in its tissues certain amino acids. This can be done, however, only if a certain group of amino acids known as essential amino acids is present in the diet.

We may define essential amino acids as amino acids that either cannot be made by animal tissues or that cannot be made rapidly enough to support normal growth and function. If these essential amino acids are present in the diet in adequate quantities, the other amino acids can be made in the tissues.

It may occur to the reader that the word "essential" is perhaps not a wise choice, since our own tissue proteins contain most, if not all, of the naturally occurring amino acids, and since so far as we know each of these is necessary for normal body structure. The word "essential" implies only that certain amino acids cannot under any circumstances be made in tissues in sufficient quantities for normal functioning and consequently must be present in the diet.

Protein Digestion

Since protein molecules are very large, they are unable to diffuse across the lining of the intestinal tract except in very minute quantities,

and hence the food protein taken by mouth cannot gain entrance into the body tissues unless certain chemical reactions known collectively as digestion take place. Gastric juice contains an enzyme known as pepsin. In the presence of this enzyme the huge protein molecules are changed into smaller molecules known as proteoses and peptones.

By likening the amino acid residues present in protein molecules to beads strung together on a string, we can imagine that in the presence of pepsin the long string of beads is chopped into several smaller strings corresponding to proteoses and peptones. After these proteoses and peptones leave the stomach, they come in contact with pancreatic juice, which the pancreas empties into the small intestine. This fluid contains a number of enzymes concerned with protein digestion. The most familiar of these is trypsin. In the presence of these enzymes the proteoses and peptones become smaller molecules known as peptides, and eventually become amino acids.

In keeping with the analogy drawn above, the strings of beads successively become shortened until in many cases only single beads (amino acids) remain. The soluble peptides and amino acids formed as a result of digestion diffuse across the membrane lining the intestinal tract and gain entrance into the blood stream, which carries them to the various body tissues.

Protein Metabolism

For our purposes we may define metabolism as the sum total of all the chemical reactions that take place in the body tissues. Some of these reactions may be compared with the burning of coal, in which energy is produced as the coal is oxidized. Physiologically, we know this type of reaction as catabolism (i.e., one in which the food molecule undergoes destruction with the production of energy).

Another kind of metabolic reaction involves the building up of new body tissue, the formation of essential substances required for the functioning of the body tissues, and the deposition of reserve material in various places in the body to be drawn on in case of need. We commonly refer to this kind of metabolism as anabolism.

The anabolism of proteins in the body involves the synthesis of all tissues, formation of hemoglobin, the synthesis of plasma proteins, body pigments, enzymes, antibodies and many of the hormones. Catabolism of proteins is a wasteful process, since it results in destruction of the protein with the formation of energy and ends in the excretion of nitrogen (chiefly in the form of urea) in the urine.

It is true that energy processes are essential for life, but sufficient energy can be derived from the oxidation of fats and carbohydrates. The prime aim of protein therapy is to supply protein for anabolic processes, and it is necessary to supply also sufficient other food to take care of the energy needs of the body in order to minimize the wasting of protein in catabolic processes.

Nitrogen Balance

An adult receiving a sufficient amount of protein in his diet eliminates in the urine and feces the same amount of nitrogen (which is, of course, derived from protein) as he ingests in the diet. In other words, if we ingest more protein than is required for anabolic processes, the extra protein will be catabolized, and its nitrogen will be eliminated from the body. Such an individual, who is excreting exactly the same amount of nitrogen as he ingests, is in "nitrogen equilibrium" or "nitrogen balance."

When, however, there is a need for the addition of extra amounts of protein to the tissues, the amount of protein nitrogen ingested will be greater than the amount of nitrogen lost from the body, provided, of course, that sufficient other food to take care of the body's energy requirements also is ingested, and assuming that the protein ingested is of good nutritional quality. When this occurs, the individual is in "positive nitrogen balance."

Positive nitrogen balance will be found, for example, in children, since they are growing and hence are adding extra protein to their tissues every day. It will be found also in persons convalescing from an illness if their diets contain sufficient protein and other foods. It will be pointed out later that protein loss from the body is excessive during any kind of illness or injury, and this lost protein must be restored.

Under circumstances where the intake of protein nitrogen is less than the loss of nitrogen from the body, the individual is in "negative nitrogen balance." This situation obviously will be found in starving individuals or in individuals who are unable for one reason or another to absorb food protein. Recent studies have indicated that it is found also following surgical or accidental tissue damage, since, for reasons as yet not completely understood, injury causes an excessive catabolism of body protein. It is the aim of protein therapy to restore a negative nitrogen balance first to a positive one and then finally, as the protein stores

of the body are replenished, to nitrogen equilibrium.

Results of Negative Nitrogen Balance

Abnormalities that accompany negative nitrogen balance include anemia, tissue oxygen deficiency, loss of weight, retarded wound healing, retarded convalescence, decreased resistance to infection (since antibodies are proteins), and tissue edema.

Edema, characterized by abnormal collections of fluid in tissues, underlies many protein deficiency states. It therefore may be worth while to discuss briefly the way in which the proteins present in blood plasma assist in regulating the exchange of fluid from the blood stream to the tissues.

The large arteries leaving the heart divide into smaller and smaller branches until finally the arterioles are formed. These small arterioles finally join the thin-walled tubular capillaries. The other end of each capillary (which is of the order of 0.5 mm. long) joins a venule. Venules combine together to form the veins that carry blood back to the heart. All exchange of fluid, foods and waste products between the blood and the tissues must occur across the capillary membrane.

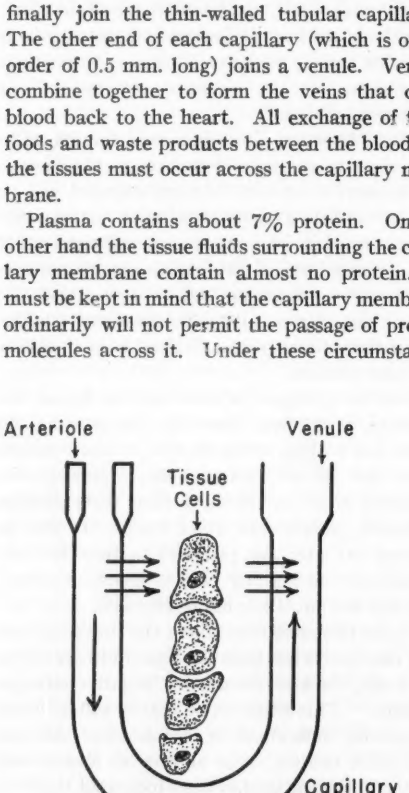
Plasma contains about 7% protein. On the other hand the tissue fluids surrounding the capillary membrane contain almost no protein. It must be kept in mind that the capillary membrane ordinarily will not permit the passage of protein molecules across it. Under these circumstances an osmotic pressure difference between the tissue fluid and the blood plasma is set up, and water attempts to flow from the tissues into the capillary. The magnitude of this pressure is approximately 22 mm. of mercury.

Now there is also a force tending to move fluid from the capillary into the tissues. This force is the blood pressure. At the arterial end of the capillary the blood pressure is approximately 35 mm. of mercury. Hence, at the arterial end fluid, carrying with it various food materials, will pass out of the capillary into the tissues, since the blood pressure (the driving force outward) is greater than the protein osmotic pressure (the driving force inward).

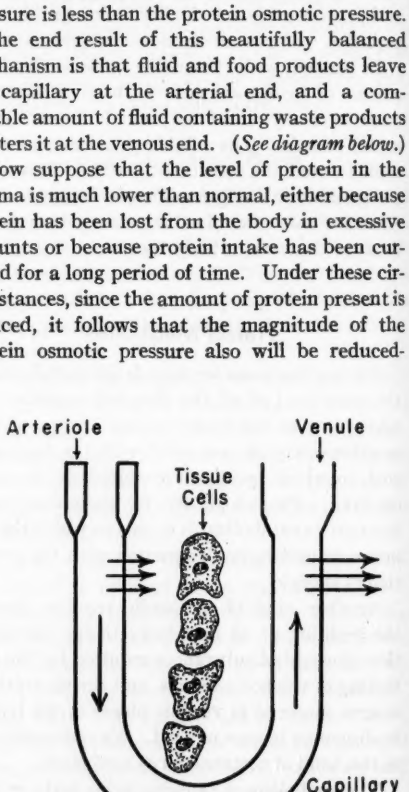
The blood pressure on the venous side of the capillary amounts to about 12 mm. of mercury. Therefore, fluid containing waste products from the cells will flow back into the capillary under normal circumstances, since in this case the blood pressure is less than the protein osmotic pressure.

The end result of this beautifully balanced mechanism is that fluid and food products leave the capillary at the arterial end, and a comparable amount of fluid containing waste products reenters it at the venous end. (*See diagram below.*)

Now suppose that the level of protein in the plasma is much lower than normal, either because protein has been lost from the body in excessive amounts or because protein intake has been curtailed for a long period of time. Under these circumstances, since the amount of protein present is reduced, it follows that the magnitude of the protein osmotic pressure also will be reduced-



NORMAL FLUID MOVEMENT



FLUID MOVEMENT IN EDEMA

As an example, suppose that this protein osmotic pressure is only 10 mm. of mercury instead of the normal 22 mm. of mercury. Under these circumstances it is apparent that fluid will leave the capillary not only at the arterial end but also at the venous end, since the blood pressure everywhere in the capillary will be greater than the protein osmotic pressure. (*See diagram.*) This, of course, will result in the accumulation of excessive fluid in the tissues, and will lead to edema.

Edema increases pressure in the tissues and interferes with the return of waste products to the blood. In addition to the mechanical effects of the increased pressure, smaller blood vessels are "squeezed" and the blood supply to the tissues is reduced. All of these factors tend to cause tissue injury and to interfere with normal processes of healing and tissue regeneration.

Causes of Negative Nitrogen Balance

DECREASED PROTEIN INTAKE.—A decreased protein intake may occur for a number of reasons. These reasons include inability of the individual to obtain sufficient protein, loss of appetite because of disease and old age, bad eating habits, and pathologic difficulties in the gastrointestinal tract that interfere with the ingestion of food. In addition, special diets used in the treatment of such conditions as diabetes mellitus, allergy, and gastric ulcer may contain insufficient protein. Diets used for the purpose of reducing weight also may be excessively low in protein. Occasionally faddists do not receive sufficient protein in the diets they choose to eat.

Special mention should be made of the importance of an adequate protein intake for older persons. At the time of birth the basal metabolic rate (rate at which food is metabolized under conditions of rest) is high (about 55 calories per square meter per hour) as compared with other periods of life. This basal metabolic rate gradually declines, and in old age may be only about 25 calories per square meter per hour. As someone has said, "We start to die as soon as we are born."

The protein requirement also is high in infancy and childhood, but as soon as growth is ended it becomes relatively constant. In other words, an older person requires just as much protein as a healthy young adult. On the other hand, the energy requirement of the older person is considerably less than that of the young adult. Hence it will be obvious that there is a tendency for older persons to ingest less food than they ingested when they were younger, and, in fact, unless this is done they must of necessity become obese. The difficulty is that if they are to maintain perfectly normal health, they must ingest the same amount of protein as the younger individual even though the intake of food is smaller. It will be apparent, then, that the diet of older people should be regulated much more carefully than has been the custom in the past, and should by some means or other be supplemented with additional protein.

INCREASED PROTEIN CATABOLISM.—The rate of protein breakdown in the tissues obviously is accelerated if there is an inadequate intake of non-protein foods. This will occur because the body will of necessity have to use a part of its protein for energy purposes if sufficient energy-yielding carbohydrates and fats are not ingested.

It has been found recently that for reasons as yet not understood protein catabolism is accelerated markedly following tissue trauma such as injuries, burns or surgery. The marked loss of protein following trauma is indicated in the table, page 494, which lists some of the results obtained by Dr. Frank Co Tui of New York University.

Obviously this type of patient will require a considerable amount of excess protein in the diet for prompt and complete recovery.

Hyperthyroidism is characterized by an increased rate of metabolism in the body, and, unless considerable excess food is ingested, will lead to a loss of tissue protein.

The rate at which chemical reactions take place in the body is increased about 7% for each degree Fahrenheit rise in temperature. For example, a patient who has a temperature of 103.6° F. has a rate of metabolism about 35% greater than normal. Since patients with fever ordinarily do not have good appetites, this means that excessive tissue destruction will take place to supply this increased energy, with a resultant loss in tissue protein.

INCREASED PROTEIN LOSS.—Hemorrhage is an obvious cause of protein loss, since each 100 cc. of whole blood contains about 20 Gm. of protein. Ordinarily protein does not occur as such in the urine. However, in many kidney diseases protein "leaks" from the blood into the urine and this is lost from the body. Certain lesions such as burns involve a loss of considerable quantities of protein-containing fluid which seeps from the injured area. Some examples of this loss are given in the table.

Pregnancy represents a normal condition in which there is a loss of protein from the mother's body. This protein, of course, is furnished to the growing embryo, is present in the fluid surround-

NITROGEN LOSS IN DIFFERENT EXUDATIVE SURGICAL CONDITIONS*

DIAGNOSIS	TOTAL NITROGEN LOST IN 24 HOURS, GM.	EQUIVALENT IN PROTEIN, GM.	EQUIVALENT IN PLASMA, CC.†
Burns, second and third degree	9.07	56.69	945
Burns, second and third degree	7.65	47.81	798
Burns, second and third degree	1.38	8.63	164
Avulsion of perineum and back	6.37	39.81	664
Radical breast	4.20	26.25	445
Abdomino-perineal resection (cancer of rectum)	6.22	38.87	644
Abdomino-perineal resection (cancer of rectum—infected)	6.97	43.56	707
Lung abscess—Pyothorax	9.57	59.81	997

* Adapted from Co Tui, F., *et al.*: *Annals of Surgery*, 121: 225(Feb.), 1945.
† The assumption is made that the protein content of plasma is 6 Gm. per 100 cc.

ing the embryo, and is required for the formation of the placenta and the enlarged uterus. In addition, the blood volume of the pregnant woman is increased, and this requires additional protein. It has been estimated that about 70 Gm. of protein should be ingested by the average normal adult per day. In pregnancy this should be increased to at least 125 Gm. daily. Lactation also causes a loss of protein from the mother's body. Even for very young infants this may amount to 10 to 20 Gm. of protein daily. Since the protein mixture in human milk has a very special amino acid composition that will not be matched exactly by food protein, it is believed to be necessary for the mother to ingest at least twice this amount of food protein in order to make up for this loss. Hence, during lactation also the protein intake should be well above normal, and preferably about 125 Gm. per day.

FAILURE TO ABSORB INGESTED PROTEIN.—In very rare instances there are diseases involving the stomach lining or the pancreas that interfere with the synthesis of the enzymes normally prepared by these organs. Under these circumstances (and it should be emphasized again that such conditions are very rare) normal protein digestion cannot take place, so that much of the protein taken by mouth is not absorbed.

In some instances also various pathologic lesions of the intestinal tract may increase motility of the intestine to such an extent that a portion of the food passes through it before complete absorption takes place. This will, of course, lead eventually to a depletion of tissue protein and the appearance of negative nitrogen balance.

Extent of Protein Loss in Disease

The amount of protein lost from the tissues in disease can be amazingly high and is, in fact, frequently much higher than the clinician may realize. Yet, unless this protein deficiency is corrected, the convalescence will be long and unsatisfactory, broken bones or other injured areas will not heal promptly, annoying decubital ulcers may appear, surgical wounds may break down, and, in fact, the patient may even die.

It may be instructive to calculate the protein requirements of a moderately depleted patient. Let us suppose that the hospital laboratory determines the amount of protein in this patient's blood plasma and finds it to be 5 Gm. per 100 cc. Ordinarily we estimate that the normal value should be about 7 Gm. per 100 cc. Hence this patient has lost approximately 2 Gm. of protein from each 100 cc. of his blood plasma. Let us suppose that his body weight is 70 Kg. (150 lb.). Since the blood plasma makes up about 5% of the body weight, it follows that this patient has approximately 3.5 Kg. or about 3500 cc. of plasma. Since each 100 cc. has lost 2 Gm. of protein, 70 Gm. of protein would be required to make up the deficiency in blood plasma protein. Now it has been found experimentally that during protein depletion protein is lost not only from the blood plasma but also from all the tissues of the body. The magnitude of this tissue protein loss, pro-

vided the loss is not acute (i.e., hemorrhage, etc.), appears to be about 30 Gm. of tissue protein for each 1 Gm. of plasma protein.* Hence in our example we may assume that this patient has lost from his body approximately 2100 Gm. (70 × 30) of protein. Since the protein he has lost is his own body protein, which has of course a special composition not identical with food protein, it usually is estimated that something like twice this amount should be fed in order to restore his tissues to normal. The physician should therefore give the patient about 4200 Gm. of protein to restore his deficit.

One other calculation also must be made. Let us suppose that we wish to restore this protein within thirty days. Now we know that even if the patient receives no protein whatever he will lose nitrogen in his urine equivalent to something like 25 Gm. of his tissue protein daily. This will occur during the thirty-day period of therapy even though he is receiving adequate quantities of protein during this time. It follows, then, that he should be fed also at least 750 Gm. (30 × 25) to compensate for this protein loss. Hence the total amount of protein to be given the patient during the 30 days will be 4200 Gm. plus 750 Gm., or 4950 Gm. If we divide this figure by 30, we find that 165 Gm. of protein should be administered daily in order to return the patient to nitrogen equilibrium in the thirty-day period. If we assume that his normal diet furnishes 70 Gm. daily, it follows that about 95 Gm. of protein in the form of some type of satisfactory supplement must be given to him in addition to his food.

The ideal protein supplement must satisfy several important criteria:

1. It must contain a high percentage of protein, and this protein must contain sufficient quantities of all of the essential amino acids.

2. It, or the diet, should contain sufficient other sources of energy so that the protein fed will not have to be catabolized for energy.

3. It should be palatable so that it is not difficult for the patient to consume the large amounts of material that ordinarily will be required.

4. It should be in a form in which it can be incorporated readily into other foods, which again will make it easier for the patient to ingest.

5. It should not cause diarrhea or other intestinal disturbances.

6. Preferably it should have a very low ash content, and particularly a low sodium content. It will be recalled that protein deficiency is characterized by tissue edema. Physiologists and clinicians have known for many years that edema formation is increased if excessive amounts of salts, particularly sodium salts, are ingested. In the presence of edema, then, most clinicians prefer to keep sodium intake at a minimum.

7. The essential amino acids should be present in properly balanced preparations in a form in which the protein containing them can be digested readily and the amino acids, therefore, absorbed. In the present stage of our knowledge, it is best to determine this by actual feeding experiments with animals. A protein that will not support normal growth and maintenance of body tissue protein reserves in animals probably will be unsatisfactory for humans, even though chemical analysis may show that all the known essential amino acids are present.

Under special circumstances soluble forms of protein will be required for therapy. If this type of supplement is required, it will be necessary to use hydrolyzed or predigested proteins, since very few tissue proteins are soluble. This hydrolysis or digestion can be accomplished by the use of enzymes, acids or alkalis. Unfortunately, all protein hydrolysates have unpleasant tastes, and many of them do not have as high nutritional values as the proteins from which they are prepared. For this reason it would seem to be preferable to use unhydrolyzed protein for the vast majority of patients, since as has been pointed out, only rarely are patients unable to digest and absorb protein taken by mouth.

An occasional patient is too ill to take any food at all by mouth. In such cases it may be necessary to inject a protein hydrolysate by vein. However, it must be realized that this is a temporary measure, and food by mouth should be started as early as possible. If solutions containing concentrations of hydrolysate higher than 3 to 5% are injected into a patient, distressing symptoms such as nausea, vomiting, and diarrhea may occur. If the product is not prepared carefully, the patient may also experience fever due to the presence of pyrogens, and may in some cases experience a sensitivity (anaphylactic) reaction. In view of the large amounts of protein ordinarily required, obviously it is difficult to give sufficient quantities of protein or protein hydrolysate by vein when the concentration used is only 3 to 5 Gm. in each 100 cc. of fluid injected.

In summary, then, in the vast majority of cases it would be preferable to administer protein supplements by mouth and to use native protein rather than protein hydrolysates. The latter type of preparation will be advantageous when the physician finds it advisable to administer protein in soluble form.

* Robert Elman: *J. Am. Dietetic Assoc.*, 18: 141, 1942.

PRESENT STATUS OF Sulfonamides

by RUTLEDGE W. HOWARD*

IMPORTANT PLACE IN THERAPEUTICS RETAINED BY SULFONAMIDES DESPITE ADVENT OF ANTIBIOTICS . . . DRUGS ARE REEVALUATED FOR PHARMACIST WITH EMPHASIS ON NEWER DEVELOPMENTS

LATE in the last century Paul Ehrlich foresaw the era of chemotherapy when mankind would have a chemical agent to destroy disease-causing organisms without harming the patient. After years of work he produced salvarsan, which is still a standard treatment for syphilis. No other important chemotherapeutic agent came to the fore until prontosil and sulfanilamide burst forth on the medical horizon. Then in rapid succession other important sulfonamides were discovered: sulfapyridine, sulfathiazole, sulfadiazine, sulfaguanidine, sulfamerazine, sulfasuxidine, sulfathalidine, and related compounds.

Some of these are better for certain purposes than others. In this discussion, it will be important to mention the drugs in relation to their clinical usage. An effort will be made to link the drug with the diseases for which it is most useful. Many of the facts presented are familiar to everyone, but a review and correlation of information is always helpful.

All the uses for the sulfonamides we know of now have not yet been established and fully evaluated. The clinical research is unending.

Absorption

When the sulfonamides are taken by mouth they are almost completely absorbed from the intestinal tract within two to four hours. Thus, it is necessary to give repeated doses on a definite schedule to maintain a fairly constant blood level. When the drugs are given by needle, the blood concentration is attained much more rapidly.

Fate After Absorption

The drugs reach the blood stream and are partly converted into acetylated forms. These are considered therapeutically ineffective and may be toxic. Average figures for acetylation of some representative sulfonamides would be:

Sulfanilamide....	20%
Sulfathiazole.....	30%
Sulfapyridine	10–90% (very variable)
Sulfadiazine.....	15%

After these changes the sulfonamides are distributed to various body tissues in amounts depending primarily upon the amount of blood supply to the tissues. With the exception of sulfathiazole they pass readily into cerebrospinal fluid, reaching a level of 50 to 65% of that present in the blood. Sulfathiazole is said to reach only about a 20% level, compared with that in the blood. The sulfonamides, it should be noted, pass readily into the red blood cells, a fact of clinical importance since the blood picture must be watched during sulfonamide treatment.

Excretion

However the sulfonamides are administered, they are removed from the body by way of the kidneys in the urine. Kidney diseases resulting in poor kidney function may reduce excretion appreciably. Keeping the urinary water output high helps in the excretion of the drug. It has been recommended that the urine volume OUTPUT should be NOT LESS THAN 1200 CC. DAILY. This may be obtained by forcing fluids. In warm weather, when the sweat glands remove much water from the body, more fluids should be taken to keep the urine volume high.

In pregnancy it is well to know that sulfonamides pass through the placenta into the fetal blood. This fact has made it possible to treat

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Paper adapted from a lecture presented at the 1946 seminar of the Northern New Jersey branch of the AMERICAN PHARMACEUTICAL ASSOCIATION.

the unborn child when necessary. Such occasions will arise when the mother's genital tract harbors the gonococcus.

Dosage for Internal Use

Many factors play a role in determining dosage if good therapeutic results are to be obtained. These may be listed briefly, although each patient requires special consideration by the physician.

Size of Dose depends upon many factors, including—

1. The type of infecting organism
2. The condition of the kidneys
3. The rate of drug absorption
4. The acuteness of the infection
5. The state of body hydration and the ability of the patient to take fluids
6. The tolerance of the patient
7. The drug concentration in the blood stream. (This last point does not indicate the clinical effectiveness of the treatment, however, and means that there is no substitute for good clinical judgment.)

Route of Dose depends upon many factors, including—

1. Contraindications for oral therapy (diarrhea, vomiting, postoperative)
2. Need for rapid use of the sulfonamides

Definite rules for dosage cannot be given for the individual patient, but we can set forth certain features about each of the better known sulfonamides with which the pharmacist should be familiar. We will discuss these in turn.

Sulfanilamide dosage: A blood concentration of 10 mg. per 100 cc. (10 mg. per cent) in adults has been found to give high therapeutic effectiveness in most infections which respond to the drug. In meningeal infections and a few others, a higher blood level has been found necessary (up to 15 mg. per cent). To obtain these concentrations, dosage has been suggested to be an initial oral dose of 3 to 5 Gm. of sulfanilamide followed by 1 to 3 Gm. orally every four hours day and night. Locally, the drug is often used in a dosage of 1 Gm. for each 10 square inches of surface involved. Limits have been proposed by competent investigators so that it is advisable at any one time for the physician to use not more than 15 Gm. on body surfaces, or 5 Gm. in body cavities.

Sulfapyridine and sulfathiazole dosage: Here we must realize that clinical judgment is more important than blood concentration. Nevertheless, it is worth mentioning that a blood level of 5 mg. per cent is considered adequate in practically all cases except meningitis where therapeutic requirements demand 10 to 15 mg. per 100 cc. of blood as an effective concentration. Translated into oral dosage for adults, this means the first dose is usually 3 or 4 Gm. followed by 1 Gm. every four hours. Intravenously, the initial dose is about the same, followed every six hours by 2 Gm.

Sulfaguanidine dosage: Here is a drug designed for use against intestinal infections. The feature quoted by independent investigators is that it can be given by mouth in doses great enough to saturate the intestinal tract without producing abnormally high blood concentrations. It has been thus used with effect against bacillary dysentery. The initial dose is recommended as being 0.1 Gm. per kilogram of body weight, followed by 0.05 Gm. per kilogram of body weight every four hours until the number of stools is five or less per day.

Sulfadiazine dosage: Good results are usually achieved by giving 3 to 4 Gm. by mouth as the beginning dose, followed by 1 Gm. every six hours thereafter. Certain patients will require a four-hour interval. It has been stated that, when sulfadiazine is given intravenously,

A. PH. A. BRANCH SEMINAR

Plans to hold another seminar as part of its program of professional activities were announced by the Northern New Jersey branch of the American Pharmaceutical Association at the October meeting. The accompanying paper was adapted from one of the professional reviews presented last spring at the first series of seminar lectures, and is presented here for pharmacists in other parts of the country.

By sponsoring the seminar, the Northern New Jersey branch has performed an important service to practicing pharmacists, returning pharmacist-veterans and the citizens of the state. It sets a high standard for other branches of the Association that may be planning similar programs.—The Editor

it is often necessary to give the drug only at twelve-hour intervals. This advantage to the patient is obviously a great one, and results from the long maintenance of effective amounts of the drug in the circulation and tissues.

Sulfamerazine (methyl sulfadiazine): In this rather recent addition to the sulfonamides we have a drug which is very similar in pharmacology and clinical usage to sulfadiazine itself.

NOTE: Incident to treatment with sulfadiazine or methyl sulfadiazine, the physician should consider the advisability of giving an alkali. Recent reports show that crystalluria due to either of these drugs may be prevented or reduced. This is most readily accomplished by giving sufficient alkali so that the urine is maintained at least as alkaline as *p*H 7.5. To achieve this end, the recommendation is to give by mouth from 10 to 20 Gm. of sodium bicarbonate in divided doses every twenty-four hours.

Succinylsulfathiazole (sulfasuxidine) is another newly added sulfonamide which should be mentioned. It is said to be so poorly absorbed from the gastrointestinal tract that only about 5% of the drug is excreted by the kidneys. Its use, therefore, is restricted by its lack of absorption from the alimentary tract. Here it helps change the bacterial flora, particularly if Shiga, Flexner, or Sonne dysentery bacilli are present at the start. The colon bacillus itself is somewhat affected, although typhoid, paratyphoid, streptococcus fecalis and B. proteus are not as susceptible.

It has been recorded that certain conditions interfere with the efficacy of sulfasuxidine. Important among these are:

1. The use of liquid petrolatum during treatment.
2. The presence of a watery diarrhea.
3. The occurrence of hard, constipated stools. In these, the bacterial action of the drug is less effective.

Phthalylsulfathiazole: Here is a further attempt to find an improved type of intestinal antiseptic. This drug's chief merit lies in its low solubility and only very slight absorption. A dose of 125 mg. per kilogram of body weight daily can cause a significant lowering in the coliform population.

Dosage for children (sulfadiazine): Dosages suitable for infants and children will vary markedly from drug to drug and from disease to disease. The short table given below may be of some help to your physicians in determining the several dosages for older children and for infants and smaller children.

Relative Effect Against Specific Infections

Now that we have covered the main points of the principal sulfonamides without going into detail, I would like to mention in a general statement that the sulfonamides should be considered most useful against certain specific organisms. Against any given infecting bacteria there will be a sulfonamide of choice. Let us briefly review this point:

For the **staphylococcus** group of infections the drugs would be used in the following order of choice:

1. Sulfathiazole
2. Sulfadiazine or sulfamerazine
3. Sulfapyridine
4. Sulfanilamide

For **hemolytic streptococcus** infections, the order of choice would be:

1. Sulfadiazine (or sulfamerazine)
2. Sulfanilamide
3. Sulfathiazole
4. Sulfapyridine

SULFADIAZINE FOR OLDER CHILDREN

BLOOD CONCENTRATION	INITIAL DOSE	MAINTENANCE DOSE
10 to 15 mg. per cent	4 Gm. (60 grs.)	1 Gm. (15 grs.), q 4 h.
5 to 10 mg. per cent	2 to 3 Gm. (30 to 45 grs.)	1 Gm. (15 grs.), q 6 h.
3 to 5 mg. per cent	1 to 1.5 Gm. (15 to 23 grs.)	0.5 Gm. (7.5 grs.), q 6 h.

SULFADIAZINE FOR INFANTS AND SMALLER CHILDREN

AGE	INITIAL DOSE	MAINTENANCE DOSE
Under 6 months	0.5 Gm.	0.25 Gm., q 6 h.
6 months to 3 years	1 Gm.	0.5 Gm., q 6 h.
3 years to 10 years	2 Gm.	1 Gm., q 6 h.

For **pneumococcus** infections, the order is:

1. Sulfadiazine or sulfamerazine
2. Sulfathiazole
3. Sulfapyridine
4. Sulfanilamide

For **meningococcus** infections:

1. Sulfadiazine or sulfamerazine
2. Sulfanilamide
3. Sodium sulfapyridine
4. Sodium sulfathiazole

For **colon bacillus** infections:

1. Sulfadiazine or sulfamerazine when infection is anywhere except in intestine.
2. Sulfathalidine when infection is in or in relation to the intestine.

U. S. production of sulfonamides in 1945 for domestic use totaled approximately 4,047,983 pounds. That this class of drugs continues to rank high in medical practice is further confirmed by the North Carolina prescription survey reported in the May issue. In the accompanying paper, Dr. Rutledge W. Howard presents an authoritative review for pharmacists on the present status of the sulfonamides.

Subcutaneous Administration

Up to the present we have discussed dosages from the standpoint mainly of the adult who takes the drug by mouth. For a moment it will be profitable to point out that the drugs may also be given conveniently and safely under the skin into the fatty tissues overlying the muscles. The majority of patients reported treated by this method received 0.5% sodium sulfonamide solutions. Isotonic sodium chloride solution was the diluent most commonly used, although certain evidence is available that sodium sulfadiazine should be diluted with distilled water. Plummer and Lockhart found that glucose solutions tended to form a loose compound with sodium sulfadiazine to render it less effective both in the test tube and in the patient. They prefer distilled water as a diluent. Although the sodium sulfonamide solutions were alkaline (ranging in *p*H value from 9.2 to 10), no untoward local reactions were reported.

Such hypodermoclysis of the sulfonamides may be run into both thighs over periods of from one to five hours. It is usually possible eventually to give the drug orally. Such administration under the skin is of advantage mostly when the patient cannot for one reason or another take the drug by mouth. It possesses the advantage over intravenous injection that the sulfonamides are more slowly absorbed and are thus more steady in their therapeutic efficacy.

Topical or Local Use

Although the large field of use for sulfonamides is in oral administration, another field of use involves applying these drugs to body surfaces. Several investigators have shown that sulfonamides may be of definite value when they are applied as an ointment or cream. There are many preparations for local application now available. Each possesses certain advantages. It would be well to mention here that the type of ointment base is of extreme importance if the sulfonamide ointment shall be used with success. Quite often the physician wishes a very high concentration of the drug locally. The ointment bases which release these high concentrations would be the emulsions—either oil in water or water in oil, and the aqueous jellies containing either pectin or bentonite, or the vanishing cream type of base.

This type of base, however, does not provide a very high degree of lubrication and would, therefore, be undesirable if the physician wishes more lubrication and a steady lower concentration of the sulfonamide at the site of application. For the higher degree of lubrication, an all-grease base containing petrolatum would be more desirable.*

Sulfonamide Fastness

In sulfonamide fastness we have a feature which is encountered commonly in the field of treatment.

The early work on the sulfonamide drugs gave the definite impression that the bacterial killing power and bacteriostatic activity of sulfonamides were inhibited by certain substances. Broken down dead tissues, degenerating bacteria, and certain tissue extracts are known to destroy the therapeutic value of the drugs. The exudate occurring on wound surfaces contains ingredients which inhibit the action of the sulfonamides. This feature was first noted and reported in cases

* It is of interest to mention here, incidentally, that penicillin, another of the newer chemotherapeutic agents, is primarily used in an ointment base which neither contains nor attracts water, since the presence of water results in a more rapid destruction of the penicillin.

INCIDENCE OF IMPORTANT TOXIC REACTIONS DURING THERAPY WITH SOME SULFONAMIDES IN ADULTS*

Toxic Reactions	Sulfanilamide		Sulfapyridine		Sulfathiazole		Sulfadiazine	
	No. Patients	*% Reactions*	*No. Patients*	*% Reactions*	*No. Patients*	*% Reactions*	*No. Patients*	*% Reactions*
Fever	2910	5%	2421	3.1%	1316	6%	4194	1.6%
Rash	3066	2.2%	3171	2%	1651	5.2%	5137	1.3%
Acute Hemolytic Anemia	1630	2%	2363	1.1%	Very rare		Very rare	
Leukopenia	1000	2%	2026	2.1%	1231	1.6%	4601	1.5%
Agranulocytosis	1000	0.1%	1444	0.8%	Rare		Rare	
Hematuria { Gross / Micro	Extremely rare		2899	4.6%	1749	4.7%	5137	1.7%
Oliguria, Anuria or Azotemia	Extremely rare		2560	2.2%	1124	1.1%	5137	0.4%
Hepatitis	1000	0.6%	Rare		Very rare		Very rare	
Total Important Toxic Reactions	11.9%		15.9%		18.6%		6.5%	

* These figures are based upon the reported incidence of toxic reactions and the author's experience, and in the instance of sulfadiazine also upon personal communications from Finland, Plummer, Flippen, Bullowa, Spink and Satterthwaite. Note the low incidence of toxicity with sulfadiazine.

when the sulfonamides were applied locally.

Failures when the drugs are given by mouth have led investigators to feel that a similar inhibition occurs within the body. Whether this resistance of the bacteria is naturally occurring or is acquired is not definitely known. Many men feel, however, that repeated exposure to quantities of the sulfonamides in ineffective doses does help create resistant strains of bacteria. Inadequate sulfonamide dosage, therefore, may render the patient much more difficult to treat.

It has been shown that once a resistant strain of bacteria is developed, it can be transmitted from one host to another, retaining its drug resistance. This would seem to be especially true in the case of gonorrhea. One plea which all interested workers are making is that the initial dose and subsequent treatment should be adequate. The world will probably otherwise experience a survival of the fittest bacteria which will not respond to the sulfonamides adequately. This is one of several reasons why sulfonamides must be administered only under close medical supervision.

A large field of research now stands open to those who are interested so that a substance may be developed which will prevent sulfonamide resistance in bacteria. An early step in this direction would be to have available a very effective substance to remove wound exudates. This would approach the problem when the drugs are used locally. Perhaps a similar type of substance can be found which could be taken internally and prevent sulfonamide resistance when the drugs are taken orally.

At this point, before we consider some of the more special uses of the sulfonamides, it will be of help to mention the toxic reactions which the sulfonamides may cause.

Toxic Reactions

Chief among these would be the renal or kidney toxicity which may occur. Crystals of the drug may appear in the urine as we have already mentioned, and red blood cells may likewise be found. Although this toxic reaction is seldom found in a serious degree, it is very important to be aware of it. The physician will usually discontinue the use of the sulfonamide under these circumstances. Occasionally, it may be possible, by reducing the dosage and by giving larger quantities of fluids, to continue the administration of the sulfonamide. The responsibility for this, however, should always rest with the physician in charge of the case.

Hemolytic anemia and a drop in the number of white cells have likewise been reported. This necessitates a study of blood during sulfonamide administration. The presence of hemolytic anemia, leukopenia or agranulocytosis means that the drug should be stopped and measures taken to remove the drug from the patient as rapidly as possible.

A somewhat more common and apparently less serious toxic effect is the presence of nausea and vomiting. Drug fever, drug rash and temporary central nervous system disorders have likewise been noted. The table of toxic reactions given above will be of interest.

These figures, together with the reports in the literature, show that sulfadiazine elicits a lower incidence of complications than any of the other sulfonamides noted in this table. Sulfanilamide is the possible exception, but this drug does not

have the beneficial effects which sulfadiazine possesses against organisms other than the hemolytic streptococcus.

Special Uses of Sulfonamides

It should be of help at this point to mention certain special uses of the various sulfonamides to help keep us fairly well up to date in this field.

Preventive use of sulfadiazine against bacterial respiratory infections: A considerable amount of work has been done during the war on the prevention of bacterial respiratory diseases by sulfadiazine. Work of great interest was reported in a publication released by the Bureau of Medicine and Surgery, Navy Department, Washington, D. C. It is publication #284.

Observations made at various Naval Training Stations indicate that chemoprophylaxis was 85% effective in preventing bacterial infections of the respiratory tract under conditions favorable to the spread of these infections. In these groups of Naval personnel, the study showed that, on the average, a saving of a day per man per month could be achieved when bacterial respiratory agents are active.

It is of interest here to report that sulfadiazine was given in this investigation to half a million men. No renal complications were detected. Reactions did occur in only 1/2 of 1% during this program. Most of the reactions were of the skin rash variety. Only two fever reactions occurred and these appeared to be reversible.

Sulfadiazine and cholera: Cholera, a scourge of the Far East in particular, has recently been reported by Commander Julius M. Amberson as being successfully treated with sulfadiazine. The cholera vaccine may be used as a preventive measure but when a patient actually is a cholera victim Dr. Amberson's work will be of extreme value. The disease is of great importance in certain areas. For example, in Calcutta, India, 3335 people had cholera. Of these, 1912 died.

Commander Amberson reports that his most effective form of treatment was the use of sulfadiazine in combination with adequate amounts of blood plasma. He reasoned that the plasma helped give the patient an effective circulating blood volume. This then gave the sulfadiazine an opportunity to reach the infected parts of the body. His results were extremely good. His work was reported recently in the *Navy Medical Bulletin*.

Prevention of rheumatic fever recurrences: In rheumatic fever we have a field of preventive medicine which can save much suffering and hardship as well as lives. Sulfanilamide, sulfathiazole and, more recently, sulfadiazine have all been used in people who have had rheumatic fever, in an effort to prevent further occurrences of the active disease. The results have been quite consistent in showing that a much smaller number of patients treated with sulfonamides preventively have a flare-up of the disease. On the other hand, control series cases receiving no preventive sulfonamide had a much higher incidence of rheumatic fever relapse or recurrences.

Summary

We have endeavored to review briefly the clinical aspects of the sulfonamide drug field. In a general way we have discussed dosage, absorption, acetylation and excretion and have outlined the comparative effectiveness of various sulfonamides in specific types of infection. Certain features of interest have received special mention, including sulfonamide fastness, the local use of sulfonamides, and sulfonamide reactions.

The preventive use of sulfonamides is still being investigated and should keep our interest alive from this standpoint. The use of sulfonamides in hitherto highly fatal diseases, such as cholera, will likewise stimulate further research.

We have entered the field of antibiotics, but in doing so we have not left the sulfonamide compounds to be forgotten. They continue to hold a high and valuable place in therapy. The extent to which sulfonamides shall continue to be used in the presence of such drugs as penicillin and streptomycin will depend in large measure upon clinical research now going on.

REFERENCES

General

1. Smith, F. G., "Sulfonamide Therapy in Medical Practice," F. A. Davis Co., Philadelphia, Pa. (A short but useful text for office use.)
2. Spink, Wesley W., "Sulfanilamide and Related Compounds in General Practice," Year Book Publishers, Chicago, Ill. Many other good texts are available.

Specific

1. Glazebrook, A. J., and Thomson, S.: "Sulfonamide Compounds and Acute Rheumatism," *J. Hygiene*, 42, 20 (January), 1942.
2. Hansen, A. E., Platou, R. V., and Dwan, P. F.: "Prolonged Use of a Sulfonamide Compound in Prevention of Rheumatic Recrudescences in Children," *Am. J. Dis. Child.*, 64, 963 (December), 1942.
3. Slocumb, C. H., and Polley, H. F.: "Prophylactic Use of Sulfonamide Compound in the Treatment of Rheumatic Fever," *Proc. Mayo Clinic*, 28, 838 (July), 1944.
4. "The Prevention of Respiratory Tract Bacterial Infections by Sulfadiazine Prophylaxis in the United States Navy," Pub. No. 284, Bureau of Medicine and Surgery, Navy Department, Washington, D. C.

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TREATING VENEREAL WARTS

We are trying to locate a product called Prodophylene (?), intended for the treatment of venereal warts. Can you help us?—O. G., California

The product you are looking for is podophyllin, the active resin of podophyllum. This should be available through any local wholesale druggist. The background for the use of this material in the treatment of soft venereal warts may be found in an article by J. V. Macgregor, *British Medical Journal*, Vol. I, page 293, 1945.

GOLD SALT PREPARATIONS

Please advise where we can obtain a product called "Lauron," which is a gold preparation for parenteral use.—E. R., Louisiana

This gold salt preparation does not appear among products accepted by the Council on Pharmacy and Chemistry, in Gutman's Drug Encyclopedia or other standard reference sources.

There are, however, a number of parenteral gold preparations on the market which may serve your need. *New and Nonofficial Remedies* lists Abbott, Merck and Searle as accepted suppliers of parenteral gold sodium thiosulfate. In addition, the Hille Laboratories (1791 Howard St., Chicago 26, Ill.) market a colloidal gold preparation called Aurol. Lakeside Laboratories (1707 East North Ave., Milwaukee 1, Wis.) also market a gold sodium thiosulfate preparation for parenteral use.

As you know, gold salts have been used rather successfully in treatment of lupus erythematosis, but other possible indications such as rheumatoid arthritis remain in doubt. In any circumstances the gold salts must be used with extreme caution because of the frequency of toxic reactions and contraindications.

FORMULA FOR CREAM SHAMPOO

We would appreciate receiving a formula for a cream shampoo.

Could you also inform us as to the method of incorporating DDT, pyrethrum, or rotenone in a cream shampoo formula?—E. D., Ohio

To make a liquid cream shampoo, it is suggested that you prepare an emulsion of cetyl alcohol or stearyl alcohol with sodium lauryl sulfate (Duponol C, Dupont), then add a sufficient amount of water and sodium lauryl sulfate to produce the desired sudsing point and concentration. The following formula will illustrate the procedure:

Cetyl alcohol	15 Gm.
Propylene glycol	10 Gm.
Beeswax	2 Gm.
Sodium lauryl sulfate	2 Gm.
Water, *q. s.*	
To make	100 cc.

Melt the fats and the propylene glycol and bring to 65° C. Dissolve the sodium lauryl sulfate in the water and bring to 65° C. Under rapid agitation add the water to the fats. When

emulsification is complete add fifty more grams of sodium lauryl sulfate dissolved in enough water to bring the total volume to 500 cc.

We would not advise incorporation of DDT. This insecticide is very slow acting, and the low concentration and brief period of application would not be effective. Possible toxicity must also be considered. It should be borne in mind that a shampoo is designed primarily to remove material from the scalp—not as a vehicle for application. An authority on cosmetics is unaware of a combination of the suggested type having been used.

WHAT IS GLONOIN?

Please send us information concerning "glonoin" including indications for its use. We are unable to obtain data from available sources.—M. M., New York

"Glonoin" is a synonym for the explosive, nitroglycerin. The medicinal product to which you refer is undoubtedly spirit of glyceryl trinitrate, also known as spirit of nitroglycerin and spirit of glonoin. This product is official in the Pharmacopœia as a 1 to 1.1% alcoholic solution of nitroglycerin.

In general, spirit of glyceryl trinitrate has an action similar to that of sodium nitrite, except that its action is more rapid, and also fleeting. Crandall has pointed out that it is not suited to conditions for which prolonged vascular dilatation is desired.

The effect of glyceryl trinitrate is to lower blood pressure. There have been reports of considerable irrational use of the drug as a cardiac stimulant. For specific information concerning indications and administration we would suggest that you contact the American Medical Association or other available sources of therapeutic information.

LIQUID FLOOR POLISHES

We would like to obtain several good formulas for liquid wood floor polish which can be easily manufactured and easily applied. Can you send the above formulas or advise us where they can be obtained?—I. F., New York

Formulas for liquid floor polishes are given in various volumes of the seven-volume compendium by Bennett called "The Chemical Formulary." This is published by the Chemical Formulary Company, 950 Third Ave., Brooklyn, New York. We believe that one of these will fill your need.

Two of the more conventional type formulas are as follows:

LIQUID FLOOR POLISH

Melt:

Paraffin wax (50–52° C.)	50 Gm.
Ceresin (58–60° C.)	10 Gm.
Carnauba wax	40 Gm.

and dissolve:

In summer, 7–9 parts in 93–91 parts of turpentine.

In winter, 6–7 parts in 94–93 parts of turpentine.

DEODORIZED FLOOR POLISH

Paraffin wax (50–52° C.)	18 Gm.
Carnauba wax	5 Gm.
Ceresin (58–60° C.)	2 Gm.
Rosin, pale	4 Gm.
Stearin	1 Gm.
Caustic soda (38° Be.)	0.5 cc.
Water	66 cc.

Boil and stir until smooth.

A water-resistant floor polish of the emulsion type is considered advantageous. The emulsifier morpholine has been used in many such formulas, and may be obtained from the Carbide and Carbon Chemical Corp., New York City.

Morpholine has a moderate volatility so that it gradually evaporates along with water from the drying emulsion polish, leaving a non-hygroscopic and water-resistant film which is said to give a high brilliance with little rubbing.

Two such formulas, given in Bennett, are quoted below. Careful attention should be given to the method of preparation, and the wax should be light-colored and the shellac fresh.

FORMULA NO. 1

a.	Carnauba wax	11.2 lb.
	Oleic acid	2.4 lb.
	Morpholine	2.2 lb.
	Water	67.0 lb.
b.	Shellac	1.5 lb.
	Morpholine	0.2 lb.
	Water	15.5 lb.

Preparation:

Melt the carnauba wax carefully with the oleic acid and maintain the temperature closely at 90° C. Stir until well mixed, add the morpholine, and stir constantly until the whole mass is quite clear. In the meantime, heat the water to the boiling point in a separate container. Add it

slowly to the hot wax mixture with steady stirring, making certain that each small portion is well incorporated before further addition. The mixture becomes increasingly viscous and should have the appearance of petrolatum when two-thirds of the water has been added.

At this point, the mixture begins to thin out, and the remainder of the water may be added rapidly. The total time for adding the water should be thirty to forty minutes. A steam-jacketed kettle and a hand-operated paddle or slow-speed, large-bladed propeller are recommended for successful production.

Allow the mixture to cool. While slowly stirring, add the shellac solution. This has been made by warming together the morpholine, water and shellac indicated in *b* above. Filter if necessary.

Another morpholine dry-bright polish is formulated as follows, using paraffin as a substitute for part of the carnauba wax:

NO. 2	
Carnauba wax	64.8 lb.
Paraffin wax	7.2 lb.
Morpholine	14.4 lb.
Oleic acid	15.3 lb.
Boiling water	430.0 lb.
Cold water	100.0 lb.

Preparation:

By observing great care in the gradual addition of boiling water up to the point of emulsion inversion (see above), a polish is prepared which is exceptionally translucent.

BRITISH OINTMENT BASE

Can you inform us where we may obtain the formula for the washable ointment base suggested by Dr. P. B. Mumford, as published in the British Journal of Dermatology and Syphilis *in 1938?—J. G., Illinois*

The formula in which you are interested appeared in a paper titled "Emulsifying Bases in Dermatology," *British Journal of Dermatology and Syphilis*, 50: 540–543, October, 1938.

A photostatic copy of this paper may be obtained from the Army Medical Library, Photoduplication Service, 7th St. & Independence Ave., S. W., Washington 25, D. C. It is our understanding that there will be no charge for this service.

If you wish to obtain a copy of the original journal, the publisher's address is H. K. Lewis & Co., Ltd., 136 Grower St., London, W. C. 1.

REPLACEMENT FOR OLIVE OIL

Has there been any official sanction covering the substitution of cottonseed oil U. S. P. for olive oil U. S. P. by the pharmacist in compounding prescriptions? We have had several inquiries regarding this matter and have been referred to you for an answer.—M. A., Pennsylvania

No official sanction could be given covering the substitution of cottonseed oil for olive oil in compounding prescriptions. It is quite true that cottonseed oil will often produce a pharmaceutically acceptable preparation when olive oil is not available, but such substitution in each instance must be approved by the physician.

In the first supplement to the *National Formulary VII* cottonseed oil was authorized as a permissible replacement for olive oil in N. F. products. So far as N. F. products are concerned, therefore, it is permissible to substitute cottonseed oil since this change was officially adopted in the formulas due to the wartime shortage of olive oil.

COAL TAR WITH MINERAL OIL

We have had trouble compounding the following prescription due to the fact that crude coal tar is only slightly soluble in mineral oil:

Crude coal tar	*2.5 Gm.*
Mineral oil, to make	*500 cc.*

What do you consider the proper way to compound this prescription?—O. G., California

Coal tar and mineral oil are so incompatible that it is frequently difficult to dispense such a mixture. If you mix the coal tar with a small quantity of hydroxystearin sulfate N. F. VIII and gradually dilute this with the mineral oil, it should be possible to obtain a product of desirable consistency. Probably 2% hydroxystearin sulfate will be sufficient, but the exact amount will depend upon the particular coal tar used.

Hydroxystearin sulfate, which is also known as sulfated hydrogenated castor oil, may be obtained from the National Oil Products Company, 1st and Essex Streets, Harrison, N. J.

SOURCE OF EMULSIFYING AGENT

Can you tell us where we may obtain the emulsifying agent Tween 80?—C. P., New York

This product is supplied by the Atlas Powder Co., Wilmington 99, Del.

Science News Capsules

ACUTE ALCOHOLICS may be treated by insulin with greater ease and comfort than by the usual method of gradually withdrawing alcohol from the diet. Small doses of insulin are administered two or three times daily before meals. This speeds up the oxidation of the blood sugar which, in turn, speeds up the elimination of alcohol itself. Successful use of the method is reported from the Ring Sanatorium, Arlington, Mass.

AN ARTIFICIAL EYE that moves like a natural eye has been demonstrated by Dr. A. D. Reudemann of the Cleveland Clinic Foundation. A fine mesh of tantalum fastened to the back of a plastic artificial eye is stitched to the eye muscles.

"HUM" OF THE UNIVERSE, the mysterious radio signals from outer space, are now attributed to interplay of free electrons in interstellar space, instead of blasts of radiation in distant stars as formerly believed.

STRONG WARNING about the "danger of addiction" to isonipecaine (Demerol) comes from Commissioner H. J. Anslinger of the Bureau of Narcotics. U. S. Public Health Service scientists and others have demonstrated its addiction properties, hence the narcotic control over Demerol recently imposed by Congress.

SKIN ANTHRAX has been successfully treated with penicillin in 25 patients at Camp Detrick, Md. Anthrax is a disease of cattle which humans get from handling infected hides or hair, thus constituting an important medical problem in the wool and leather industries.

THE MESOTRON, considered the key to the atomic nucleus, has finally been measured with some assurance of accuracy. After cloud-chamber analysis of 26 mesotrons, University of California physicists reported the mass as 202 times that of the electron, very close to the theoretical figure which had been assigned to it.

MENTAL OR NERVOUS ILLNESS will strike 10,000,000 Americans sometime during their lives, according to a U. S. Public Health Service estimate. To help meet the situation Congress enacted the National Mental Health Act, establishing a National Institute of Mental Health, grants-in-aid for research and personnel training, and a National Advisory Mental Health Council.

ATOMIC ENERGY POWER PLANTS would cost four times as much to build as coal-burning plants, but would generate power at a slightly cheaper cost, Westinghouse engineers estimate. Application of atomic energy to production of electricity is "much closer at hand than most people think," they maintain.

SAVING FISH from furunculosis, strangely enough the most destructive disease in fish hatcheries, is a new job of sulfamerazine. U. S. Fish and Wildlife Service experiments offer the first real hope of effective treatment.

A GREAT WALL in the mountains of northeastern Paraguay, 4500 feet long and more than 120 feet high, may hold the secret of a past civilization. Built of huge blocks of polished red granite, the structure is considered an excellent work of engineering. Drawings, and signs that may be hieroglyphics, are expected to yield valuable information to archeologists who will study the site.

A GROWTH HORMONE from the pituitary gland is considered the single substance responsible for the basic mechanism of growth by University of California scientists, following extensive experiments. This opens a new field for study of some fundamental life processes, but clinical application is not yet in sight.

FAMINE would join the atomic bomb and man-made pestilence to make World War III an apocalyptic horror. Complex organic chemicals, like 2,4-D, have been developed which will kill or stunt field crops when sprayed from planes.

SURPLUS BULLET-PROOF JACKETS from the Army will be put to good use by U. S. oil prospectors in the jungles of Colombia where they are targets for the primitive arrows of natives.

ETHER USED INTRAVENOUSLY can relieve diabetic patients of the extreme pain due to ischemia which often occurs after diabetes has been controlled for many years by insulin. Noting that ether causes increased blood circulation when given as an anesthetic, Dr. Robert A. Katz of the Touro Infirmary,

New Orleans, made tests on himself to determine the safety of ether injections. A local anesthetic added to the ether lessens the pain, and peanut oil may be added to prolong the effect.

CANCER OF THE LARYNX is being cured in an increasing number of cases by radium or x-rays, where laryngectomy was formerly the only hope of saving the patient. In a series of 118 cases, five-year cures were achieved in 42% of the patients, and three-year cures (the time elapsed since treatment) in 39%, Dr. Max Cutler of the Chicago Tumor Institute reports. "Concentration radiotherapy," as the treatment is called, involves the use of the most intense radiation practical.

S/V SOVABEAD, a new desiccant (Socony Vacuum Oil Co.), offers aid wherever lower humidity is needed in industry or homes. A few beads of the material in a salt shaker prevents caking. A handful in a tool box avoids rusting. As compared with silica gel, the material is extremely hard and durable, and does not easily become powdered.

PARA ARSENOSOPHENYLBUTYRIC ACID has been successful in the treatment of 319 human cases of African sleeping sickness. It was estimated that 90% of the early cases can be cured within a period of one week if the standard total dosage is used, whereas other drugs may have to be continued for as long as twelve to fifteen weeks. Intramuscular injection proved to be as effective as intravenous injection.

FURACIN, a yellow powder derived from the hulls of oats, appears to be another valuable new drug. Believed to be bactericidal as well as bacteriostatic, this nitrofuran has been used in the treatment of infected ulcers and superficial skin infections with "very good" results. It is available as an ointment (Eaton Laboratories), and may eventually be offered in oral form if clinical work confirms laboratory experiments.

PNEUMONIA DEATHS had dropped to less than 4 out of every 100 cases by 1942, thanks to the advent of the sulfonamides. In the pre-sulfa years, 1935–37, the mortality rate was about five times as great.

COTTON COLORED BY NATURE has been produced experimentally in Russia by careful plant breeding. These naturally colored cottons are said to fade less than artificially dyed fibers, are not subject to deterioration resulting from dying and are more resistant to wilt.

BACTERICIDAL RADIATION and the emission of ozone from a tiny ultraviolet lamp will be used to assure odorless refrigerators, improve sanitation, enable longer preservation of food, and check the growth of mold and bacteria on the food. The lamp is about the size and shape of an automobile headlight bulb, a miniature relative of the commercial Sterilamp.

ENCEPHALITIS may be caused by the same virus which causes fever blisters and cold sores. During the first world war some scientists believed this, but only recently has confirmatory evidence been forthcoming.

WORLD'S LARGEST cyclotron and synchrotron and a uranium pile for producing radioactive elements for laboratory work will be constructed at Camp Upton, N. Y., by Associated Universities, Inc. Pure research looking to peacetime use of atomic energy is the main objective. About a dozen buildings will house the staff of nearly 1000 technical and nontechnical personnel.

NESA, commercial name of a permanent transparent coating used on airplane windshields, conducts an electric current which clears the glass of ice and fog.

COLISTATIN, a new antibiotic of possible practical significance has been discovered in Russia. It is produced by a bacillus found in black earth or chernozem soils.

BACTERIOPHAGE preparations are being used in Russia to treat infected wounds. At the All Union Congress of Surgeons held in Moscow recently it was reported that the technique had proved itself in a series of more than 1000 patients. Local applications to infected soft-tissue wounds gave positive results in 82.9% of such cases. Bacteriophage may also be used as a dressing to prevent complications.

LILLY DIGEST . . .

OPERATING STATEMENTS OF 1945

SALES AND PRESCRIPTION PRACTICE REACHED A NEW HIGH BUT PROFITS DID NOT KEEP PACE, MERCHANDISE STOCKS REFLECT EXCESSIVE BUYING

PRESCRIPTION revenue, typically one-sixth to one-eighth of total income in a retail pharmacy, may produce more than one-fourth of the total gross margin realized from all sales. Thus concludes the forthcoming *Lilly Digest* of an analysis of prescription department activities in 677 pharmacies which supplied detailed data on their 1945 operation. The favorable returns from a prescription laboratory stem from the fact that the professional services involved produce margins which may be as much as 60% of sales, whereas average, total gross margins in pharmacies are now about 33% of sales.

The average revenue derived from prescriptions in the 677 pharmacies was $8477 in 1945, an increase of about 17.4% over the previous year. Prescriptions represented 14.1% of total volume.

This income represents, on the average, 7064 prescriptions annually, or 136 per week. Assuming that these pharmacies maintained a gross margin of 55% or $4662, it may be seen that professional services can justify the continuous attention of a pharmacist. Routine work could then be shifted to helpers who do not have professional qualifications. The owner who is a pharmacist will thus have sufficient time to supervise operation of the pharmacy and take care of his professional duties. He can devote attention to further development of the services for which he was trained and which are his main purpose in the community.

Pharmacy owners today have an unusual opportunity to hold prescription receipts at present levels, the *Lilly Digest* points out. More people than ever before have been consulting physicians about their ills. More physicians have been writing more prescriptions than ever before. It will take hard work and persistent, cooperative effort between pharmacists and physicians, however, to maintain the trend toward rational medication under medical supervision. When deflation sets in, there will be a natural tendency for people to turn once more to home remedies and other concoctions.

Despite current inflation in most fields, prescription prices have remained stable. The average price was $1.20 in pharmacies which reported prescription prices in the Lilly study, compared with an average of $1.10 for the previous year. Part of this increase would no doubt be accounted for by the relatively high cost to the pharmacist of some new medications.

The geographic variations in average prescription prices were as follows:

GEOGRAPHIC VARIATIONS IN PRESCRIPTION PRICES

New England States	$1.17
Middle Atlantic States	1.17
East North Central States	1.34
West North Central States	1.18
South Atlantic States	1.05
East South Central States	1.01
West South Central States	1.20
Mountain States	1.21
Pacific States	1.41
United States	1.20
Canada	1.28
Average	1.20

The variations in average prescription prices by size of city were small and show no consistent pattern.

VARIATIONS IN PRESCRIPTION PRICES BY SIZE OF CITY

Under 5000 population	$1.10
5000 to 20,000	1.27
20,000 to 50,000	1.23
50,000 to 100,000	1.33
100,000 to 500,000	1.22
Over 500,000	1.28
Average	1.20

Of each 100 prescriptions filled in these pharmacies during 1945, usually about 59 were being filled for the first time. The other 41 were refills. Thus the pharmacy owner who keeps an account only of prescriptions filled for the first time may underestimate his prescription volume by more than 40%. The ratio of refilled prescriptions to total prescriptions varies somewhat geographically, ranging from 52.2% refills in the New England states to 31.6% in the West South Central states.

TABLE 1—MONTH-TO-MONTH FLUCTUATIONS IN PRESCRIPTIONS BY NUMBER FILLED PER PHARMACY

STORES COMPOUNDING IN 1945:	J	F	M	A	M	J	J	A	S	O	N	D
1 to 5 prescriptions daily....	100	98	110	99	95	90	87	94	93	100	109	130
5 to 10 prescriptions daily....	100	94	102	95	94	85	79	83	82	94	103	124
10 to 20 prescriptions daily....	100	95	104	95	95	88	87	89	89	97	102	122
20 to 40 prescriptions daily....	100	96	105	94	94	88	87	91	91	100	102	122
40 up prescriptions daily.....	100	93	102	92	92	88	85	88	88	96	95	113
Average.....	100	95	104	94	94	88	85	89	89	98	99	119

A commonly heard fallacy is that most prescription refilling occurs in a few winter months. This is not borne out by the Lilly study, in which 482 of the 677 pharmacies supplying separate reports on the prescription department also indicated the number of new and refilled prescriptions month by month. In these 482 pharmacies the fluctuation in the proportion of refills to total prescriptions was greatest, on the average, between the months of December and January. Even here the variation was only 3.2%.

Seasonal variations in the total number of prescriptions filled are also apt to be greatly overestimated. The average fluctuations in pharmacies reporting to Lilly, distributed throughout the country, were tabulated as shown in Table 1.

Contentions that the operation of a prescription laboratory calls for an investment in equipment, supplies and stock out of all proportion to the prospective income appears to be correct only if the number of prescriptions filled averages 5 or less daily, according to the survey data.

Of the 677 pharmacies that supplied reports for 1945 on their prescription departments, there were about 22% that filled an average of 5 prescriptions or less daily. These owners had a return of only $1.50 in 1945 for each dollar invested in their prescription department stocks—a higher figure than in former years but still distressingly small. If the gross margin on prescriptions averaged 50% of the prescription price received, the average rate of turnover was once every sixteen months; if the gross margin was 60%, the turnover was once every twenty months.

Pharmacies filling 20 to 40 prescriptions daily received $5.12 for each dollar invested in prescription department stock, and would have a turnover of 2.5 times per year assuming a 50% gross margin. Those filling 40 or more daily had revenues of $7.09 per dollar invested, with a turnover of 3.5 times assuming an average prescription margin of 50%. The relationship between investment and prescription sales-dollar during the years 1940 to 1945 for prescription practices of various size are shown in Table 2.

There is evidence that in 1945, as in earlier years, the pharmacies with the busiest prescription laboratories were the pharmacies in which over-all profits were the highest. This is to be expected. An idle prescription department earns no profits for anyone. A pharmacist who is not busy at his profession in his pharmacy cannot expect to obtain the greatest possible return from his training and experience. As the *Lilly Digest* points out, it is also probable that the necessarily high standards and professional pride in a busy prescription laboratory have a very decided tendency to put the rest of the pharmacy's departments on the same high plane. The survey sup-

TABLE 2—RATIO OF PRESCRIPTION SALES-DOLLAR TO EACH DOLLAR INVESTED IN PRESCRIPTION STOCK, ACCORDING TO NUMBER OF PRESCRIPTIONS FILLED

STORES COMPOUNDING:	1940	1941	1942	1943	1944	1945
1 to 5 prescriptions daily.....	$1.11	$1.29	$1.43	$1.41	$1.25	$1.50
5 to 10 prescriptions daily.....	2.13	2.28	2.34	2.32	2.32	2.75
10 to 20 prescriptions daily.....	2.84	3.16	2.86	3.14	3.07	3.92
20 to 40 prescriptions daily.....	3.60	4.04	3.89	4.44	4.03	5.12
40 up prescriptions daily.....	4.49	4.37	4.08	5.80	5.04	7.09
Average.....	2.80	3.10	3.12	3.53	3.47	4.53

TABLE 3—AVERAGE NET PROFIT PER DOLLAR INVESTED IN ALL MERCHANDISE STOCKED IN RELATION TO PRESCRIPTION VOLUME

STORES COMPOUNDING:	1940	1941	1942	1943	1944	1945
1 to 5 prescriptions daily	21¢	32¢	43¢	52¢	56¢	51¢
5 to 10 prescriptions daily	27¢	34¢	45¢	56¢	56¢	56¢
10 to 20 prescriptions daily	36¢	46¢	51¢	70¢	62¢	54¢
20 to 40 prescriptions daily	43¢	43¢	57¢	69¢	75¢	75¢
40 up prescriptions daily	27¢	25¢	50¢	$1.02	75¢	71¢

plies evidence to support these assumptions as shown in Table 3.

The over-all sales in pharmacies in 1945, including all departments, was 18.6% higher than in 1944, or an average of $62,038. In 1932 average sales were only $24,454, and in 1942 were $40,514. The 1945 sales figures, and other data given below, are averages from 1037 pharmacies reporting, including the 677 pharmacies which supplied detailed information on prescription department activities previously discussed.

When sales are rising in a pharmacy, profits are likely to go up at even a more rapid rate. No such thing happened in 1945. Expenses increased 22.6% over 1944 as against the increase in sales of 18.6%. This resulted in a slight decrease in the rate of profit.

Another disturbing factor was the increase in merchandise stock reported. The average value of all stock per pharmacy was $9459, or 50% above the 1943 total. This increase in stock during the past three years has resulted in a slowly declining average annual rate of turnover.

Increases in sales ordinarily do not call for increases of the same proportions in merchandise stock. The increases in stock in the past three

TABLE 4—AVERAGE COSTS AND PROFITS OF PHARMACIES IN 1945 AND 1944

	1945		1944	
Sales		$62,038—100.0%		$52,297—100.0%
Cost of goods sold		41,565— 67.0%		35,283— 67.5%
Gross Margin		$20,473— 33.0%		$17,014— 32.5%
Expenses:				
Proprietor's or manager's salary	$4342—7.0%		$4182—8.0%	
Employees' wages	5273—8.5%		3660—7.0%	
Rent	1860—3.0%		1308—2.5%	
Heat	245—0.4%		215—0.4%	
Light and power	372—0.6%		260—0.5%	
Taxes (except on building, income, and profit) and licenses	498—0.8%		425—0.8%	
Insurance	195—0.3%		157—0.3%	
Interest paid	61—0.1%		52—0.1%	
Repairs	253—0.4%		155—0.3%	
Delivery	64—0.1%		55—0.1%	
Advertising	311—0.5%		262—0.5%	
Miscellaneous	684—1.1%		702—1.3%	
Estimated total depreciation except on buildings	251—0.4%		265—0.5%	
Bad debts charged off	59—0.1%		55—0.1%	
Telephone	128—0.2%		156—0.3%	
Total Expenses		$14,596— 23.5%		$11,909— 22.7%
Net Profit		$ 5,877— 9.5%		$ 5,105— 9.8%
Value at cost of merchandise stock		$ 9,459		$ 7,926
Annual rate of turnover of merchandise stock		4.4 times		4.5 times

TABLE 5—COMPARISON, BY SIZE OF PHARMACY, OF NET PROFITS EARNED IN 1945 IN 1037 PHARMACIES

	Under $10,000	$10,000 to $20,000	$20,000 to $30,000	$30,000 to $50,000	$50,000 to $100,000	Over $100,000
Number of Pharmacies of Each Size	15	55	144	305	372	146
Operating at a loss	20%	5%	5%	3%	3%	2%
Net profit less than 2% of sales	13%	11%	8%	7%	6%	6%
Net profit 2% to 4%	20%	10%	14%	12%	13%	21%
Net profit 5% to 9%	13%	21%	31%	30%	30%	36%
Net profit 10% and over	34%	53%	42%	48%	48%	35%

years are probably the result of buying for more than current needs and may even reflect some speculative buying.

The profit rate of 9.5% shown in Table 4 is the average for all 1037 pharmacies included in the report. An analysis by size of store (Table 5) shows that profits of this amount were the general rule in pharmacies of virtually every size, with the outstanding exception of those with sales under $10,000 annually. The general inability of small pharmacies to make a satisfactory profit in an unusual year such as 1945 illustrates the vital necessity of choosing a suitable location. This is no consolation to the owner who has all of his capital tied up in a hopelessly unprofitable location.

Under present conditions most of these owners would be better off if they abandoned their pharmacies and started again where conditions were better, the *Lilly Digest* concludes. In many instances they would do better at the present time working as employee pharmacists.

Other pharmacies are handicapped by the unwarranted increase in merchandise stock. High average gross margins which may result from quantity buying do not necessarily result in high average net profits per dollar of sales. The upward trend in net profit per dollar invested, as the rate of turnover increases, has been demonstrated by the Lilly study* all through the war years. It appeared also in the prewar years. It is convincing evidence of the correctness of buying only for current needs.

* Copies of the complete *Lilly Digest* for 1945 may be obtained on request from Eli Lilly and Company, Indianapolis 6, Ind.

TYPHOID RESPONDS TO BACTERIOPHAGE

Type specific bacteriophage, a virus-like agent, offers a promising and safe procedure for treatment of typhoid fever, according to a preliminary report from the Los Angeles County General Hospital. In a series of 56 patients the mortality was 5%. For many years the death rate has been about 10%.

It is reported that bacteriophage, considered a parasite of bacteria, has been used for the past ten years in the Los Angeles hospital for treatment of patients whose *Eberthella typhosa* organisms could be typed. The number of bacteriophages is legion but each differs in its ability to attack certain types of bacteria. Each patient was given the specific phage which would attack his own organisms.

The following results were immediately noted: (1) negative blood cultures twenty-four hours after treatment, (2) absence of fever, (3) immediate clinical improvement.

The specific bacteriophage in a dextrose solution was administered by intravenous drip over a period of four to seven hours. This was usually followed by a moderate chill lasting approximately thirty minutes. After the chill the physicians noted that the temperature began to mount and reached a peak of 105° to 107° F. within three to six hours. The temperature returned to normal within $9^1/_2$ to 24 hours after treatment was started and in most instances remained normal.

Five physicians associated with the Los Angeles County General Hospital reported the clinical study: Evelynne G. Knouf, Walter E. Ward, Paul A. Reichle, A. G. Bower, and Paul M. Hamilton.

—*J. Am. Med. Assoc.*, 132:134, 1946

The Hospital Pharmacist

SURVEYING THE SURVEY

by LEO. F. GODLEY
AMERICAN SOCIETY OF HOSPITAL PHARMACISTS

THE Pharmaceutical Survey, a long-range, nation-wide study of pharmacy to be conducted by the American Council on Education, has begun to break ground. Dr. Edward C. Elliott, director of the Survey, was very much in evidence at the recent A. PH. A. convention and spoke at several sessions, including a joint meeting of the American Society of Hospital Pharmacists and the American College of Apothecaries. It was readily apparent that his energy, incisiveness and capability are what such a movement must have to succeed.

It was also apparent that pharmacists found it difficult to face some of the demands and implications of his questions. But he gave fair warning that he will not be satisfied with half truths and stereotyped answers. As he walked from the meeting room, he left a friendly and welcome challenge: "The hospital pharmacists haven't heard the last of me yet."

With such a movement in progress—a movement which may mark a time from which succeeding annals of pharmacy will be reckoned—hospital pharmacy must be ready to offer full cooperation and to record its voice in the data gathered by the Survey. On the Survey's advisory committee we are well represented by Donald A. Clarke of the New York Hospital.

The results of the Survey will have, potentially, a far-reaching importance. Their ultimate significance will of course depend upon the extent to which we shall act upon them. It may be well to review some of the Survey's aims and examine their implications for hospital pharmacy.

One of the first studies will pertain to the practices of pharmacy colleges as to the selection, admission, guidance and training of students. From current reports it may be assumed that many schools have applications for admission far exceeding the teaching facilities. We favor selective admission as a logical means of helping assure the caliber of hospital pharmacist—or any other kind of pharmacist—needed to supply our health services adequately.

Eventual policies in regard to student selection, admission and guidance undoubtedly will be influenced by conclusions from another phase of the Survey study: supply and demand for trained pharmacists. As far as institutional pharmacies are concerned, it should become obvious that there are far too few pharmacists who are properly trained, and equally few available for this training. The dearth is evidenced in all localities and it is becoming more dire as hospitals increase their bed capacity, as new hospitals are built, as state boards of pharmacy extend the pharmacy law to include hospital pharmacies, and as governmental branches become more pharmacy conscious.

Better vocational guidance would no doubt help those students inclined toward the hospital type of practice to crystallize their thinking and to make professional plans leading to hospital pharmacy. That more students do not become interested in hospital pharmacy may lie to some extent at the door of present discriminatory regulations against full credit for hospital pharmacy experience in meeting licensure requirements. Thus a number of students who might otherwise gain experience and interest in hospital practice can logically be expected to obtain their "intern" training in the retail pharmacy which will be honored by state pharmacy boards.

Fortunately the relation of requirements for licensure to the training program and practical

needs will also be studied by the Pharmaceutical Survey. An exploration of this subject could be expected to demonstrate that hospital training actually equips the interning pharmacist in excess of legal requirements, even though such training is recognized by only a few state boards.

We look forward to the Survey focusing attention on the state boards, particularly in regard to licensing examinations. They are notorious, in our opinion, for inadequately measuring the qualities of the modern pharmacist. The writer speaks from first-hand as well as second-hand knowledge, having had occasion to become licensed by examination in three different states. We can truthfully say that the examinations were all inadequate in scope, in representation, and in timeliness.

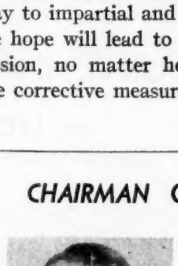
In turning to an examination of qualifications of faculty members and conditions of faculty service in pharmacy colleges, the Survey will, we hope, make some evaluation of how well education meets our practical needs. It is our personal feeling that at least a greater part of a faculty should actively engage in professional practice from time to time—without sacrificing academic achievement. How, indeed, could a teacher instruct in hospital pharmacy unless he is or has been actively engaged in hospital work.

The Survey will also give attention to methods and means of training the type of pharmacist now required for rapidly growing pharmaceutical industries and for pharmaceutical research. Most hospital pharmacists would probably agree that basically the requirements for all branches of the profession are equal at the undergraduate level. We would like to see consideration given to: (1) more uniformity of curricula in schools, after careful study to delete outmoded material and to add new and necessary teaching aids; (2) addition of another year to the undergraduate program to meet today's needs, and of course the development of a strong postgraduate program for specialization; (3) establishment of facilities to bring out the pharmaceutical interests and capabilities of the student. Failing to do so we should resort to the humane and kindly act of encouraging the student to pursue a more agreeable line of university study.

Of particular interest to practicing pharmacists will be the Survey's analysis of prescriptions to determine the professional knowledge necessary for today's pharmacist. A survey of the prescriptions in a hospital's out-patient and in-patient files should inform the Survey workers adequately as to the scope of the technical knowledge in pharmacology, physiology, chemistry and bacteriology that the hospital pharmacist should command. We welcome such a survey. We believe that a study of hospital practice will show a type of pharmacy that fulfills the objectives of pharmaceutical education. In fact we can show a brand of pharmacy that proves some undergraduate pharmaceutical education inadequate.

We look forward to the Survey's report on these and other phases of present-day pharmacy. Editorial opinion and introspection will give way to impartial and objective conclusions that we hope will lead to united action by the profession, no matter how unpleasant or difficult the corrective measures appear.

CHAIRMAN OF THE A.S.H.P.



HANS S. HANSEN

HANS S. HANSEN, chief pharmacist at Grant Hospital, Chicago, has been installed as the new chairman of the American Society of Hospital Pharmacists, an A. PH. A. affiliate. To the leadership of the youthful Society he brings a mature and broad background covering three decades of experience in various branches of the profession.

Born in Iowa of Danish parents, Hans developed an early interest in the health professions under the guidance of his father, a Lutheran minister turned physician—a man who ministered to the ills of Cedar Falls citizens during the last forty years of his life.

With this environment, it was natural that the son should have entered Northwestern University School of Pharmacy, graduating in 1913. Following sixteen years of retail practice in Iowa, Mr. Hansen became a pharmaceutical manufacturer's representative in Wisconsin, from whence he entered hospital practice.

As pharmacist at Grant Hospital for the past eight years, Mr. Hansen has contributed a number of articles to the professional literature and recently served on the faculty of the first Institute of Hospital Pharmacy. He is a member of the AMERICAN PHARMACEUTICAL ASSOCIATION, as well as the American Society of Hospital Pharmacists, and served the latter organization during the past year as chairman of the organization committee.

MIDWEST HOSPITAL PHARMACY

by WILMA K. MAUS, Chief Pharmacist
MERCY HOSPITAL, COUNCIL BLUFFS, IOWA

NINE years ago a small group of hospital pharmacists, mainly from Omaha, Lincoln and Council Bluffs, met and organized the "Hospital Pharmacists of the Midwest." Though still a small group, its members have found it of increasing value through exchange of ideas and favorite formulas and discussion of mutual problems. Possibly the greatest advantage arising from the organization has been heightened morale of the individual pharmacists and inspiration to improve pharmacy service in their respective hospitals. Having recognized the benefits of organized pharmacy, the Hospital Pharmacists of the Midwest was one of the first groups to affiliate with the American Society of Hospital Pharmacists.

Because our organization is small, it has been difficult to complete some of the projects undertaken; however, our aims are essentially the same as those of the American Society of Hospital Pharmacists. Among the present projects of the organization is the promulgation of a set of minimum standards for hospital pharmacies intended for midwest institutions that do not offer internships. By introducing these standards it is hoped that hospital administrators will realize the extent of services possible through the pharmacy and will give their pharmacists the opportunity to utilize fully their training and ability. Thus, it is the aim of Hospital Pharmacists of the Midwest to give this area improved pharmacy service in its hospitals and to give hospital pharmacists increased professional recognition in their work.

Encouraging employment of a full-time pharmacist in hospitals is another aim of the organization. By publicizing the fact that an expert is required to insure economical management in the purchasing, storage and handling of drugs and to provide the patient with proper pharmaceutical service, we hope that even the small hospitals in this area will be stimulated to employ a full-time pharmacist.

Our hospital, with a capacity of 150 beds, might be considered typical of the twelve hospitals whose pharmacists are members of the Hospital Pharmacists of the Midwest.

Mercy Hospital is a general hospital operated by the Sisters of Mercy. More than 4000 prescriptions are filled each month for the hospitalized patients by one pharmacist, who is aided by a non-registered assistant. No prescription medications are stocked on the wards and floors except for a small supply of emergency ampuls. Though this practice necessarily increases the amount of work in the pharmacy, it makes it possible to operate efficiently with a smaller inventory than would otherwise be required. Since medications are not issued in any department at a flat rate, this method facilitates accuracy in charges to patients. Also, deterioration and waste of drugs are practically eliminated.

To aid in efficient purchasing, a card index giving date of purchase, manufacturer, amount of purchase and cost of items is maintained. This, coupled with personal contacts with staff physicians, particularly in reference to new or unusual drugs, makes it possible to keep an adequate stock, yet largely eliminates an accumulation of dead items which so frequently results from uncontrolled purchase of drugs for trial use by physicians. By judging from the entries in the index, the trend of demand for particular drugs can be predicted.

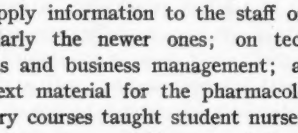
In addition to the perpetual narcotic and alcohol inventories, a general financial record is kept. The number of prescriptions filled, the total charges, stock supplied to the various departments, medications for student nurses, and supplies which are sent to other institutions operated by the Mercy Order are recorded daily. This concise record is intended only as a source of information for the pharmacist since the auditor prepares monthly reports on each department. However, in hospitals where such records are not kept by the business office, this could serve as a medium

through which the pharmacist could justify desired improvements in the pharmacy.

Manufacturing can cut down the operating expenses of a hospital pharmacy to a considerable extent, but time is a limiting factor. Since ward and department supplies do not include prescription items in our institution, it has been possible to cut "drug basket days" to four a week. This gives two days which may be devoted to manufacturing.

As an educational center in the hospital, the pharmacy has tried to establish a worth-while library including required and recommended books for hospital pharmacies and two literature files. One is an alphabetized file of drug pamphlets and the other contains articles clipped from various professional journals and the house organs of pharmaceutical manufacturers. These files supply information to the staff on drugs, particularly the newer ones; on techniques, formulas and business management; and augment text material for the pharmacology and chemistry courses taught student nurses by the pharmacist. A carefully cross-indexed card system started a year ago has proved valuable. This eliminates wasting time hunting through old journals for articles and also saves much space which was formerly devoted to storage of journals. Desired information is now quickly available with a great saving in time.

Through the medium of the Hospital Pharmacists of the Midwest various procedures, such as those mentioned, may be discussed, considered for adoption and improved upon in member hospitals having similar requirements. Personal interchange of professional data is one of the advantages of organizational work that benefits the pharmacist, his institution and the patient.



N. J. HOSPITAL PHARMACISTS MEET

At a recent meeting of the New Jersey Society of Hospital Pharmacists held at Rutgers College of Pharmacy, the following officers were elected: Lena Cutler, president; Charles Seal, vice-president; Jennie Cutler, secretary; and Grace Huber, treasurer.

During the meeting Albert W. Moore discussed the constitution and by-laws.

Hospital Queries

CONDUCTED FOR THE JOURNAL

by JOHN J. ZUGICH

When submitting professional problems please give pertinent details. Inquiries receive personal replies, from which subjects of general interest are selected for discussion in this column. Address correspondence to the Journal, 2215 Constitution Ave., N. W. Washington 7, D. C. This service covers all phases of hospital pharmacy practice, although prescription inquiries are referred to the "Prescription Information Service" department.

WATER PURIFICATION

We need information on a unit to supply water comparable to distilled water to replace a poorly functioning still in our pharmacy. Some literature has mentioned the use of resins for water purification. Do you know the source of such units?

We believe you refer to the use of ion-exchange resins. It must be remembered that units supplying this mineral-free water do not supply a product sufficiently pure for parenteral use. Two sources of such units are: Illinois Water Treatment Co., Rockford, Ill., and the Barnstead Still and Sterilizer Co., Inc., 2 Lanesville Terrace, Forest Hills, Boston 31. The former lists the unit as a "deionizer,' the latter as a "demineralizer."

SQUARE FEET PER HOSPITAL BED

Our drug room floor space is to be expanded with new construction which will give our hospital 410 beds. At present the hospital has 250 beds and the drug room has 635 square feet of space. How many square feet might be requested for the new unit?

Hospital architects have set "rule-of-thumb" space allotments for various hospital departments. A measure at the moment is five square feet per hospital bed as answering basic requirements for the pharmacy. If manufacturing in quantity or preparation of bulk intravenous fluids is planned, the footage might be increased to 10 square feet per hospital bed. For your new 410-bed institution, the pharmacy might occupy at least 2050 square feet.

Your use of the term "drug room" prompts a word on a disappearing name. It should be dropped as soon as feasible since it is considered

outmoded for obvious reasons. The term "pharmacy" is a much better designation.

GIFT SHOP IN PHARMACY?

I serve an institution associated with a university medical center on the outskirts of a large city of 750,000. Overnight accommodations to relatives and visitors of patients are to be offered in a new building being planned, since it is several miles to any shopping or hotel accommodations. The administrator plans to offer a "convenience" service to these persons by having a drug sundry and gift shop in the building, not to include any prescription work. As chief pharmacist, what would be the proper attitude on this "extra-curricular" activity of the hospital pharmacy?

It would be advisable to convince the administrator that this is not an activity within hospital pharmacy practice, because even though its location is far removed from commercial enterprises it may indirectly compete with them. It could be operated on a concession basis by a qualified local concern; or it could be managed by some charitable organization with volunteers as workers. The profits accrued in the latter instance would be given to the institution and distributed much as "Community Chest" appropriations. One large hospital distributes profits of such an enterprise to a "Crippled Children's Fund." Although the exact scope of the proposed shop is not clear, it seems to have so little relation to pharmacy that it might just as logically be placed under surgery or any of the other departments.

A TEXT IN HOSPITAL PHARMACY

Is there a text on hospital pharmacy available? What schools offer courses leading to a major in hospital pharmacy?

There is no complete text on hospital pharmacy available at this writing. Remington's *Practice of Pharmacy* has an excellent section devoted to hospital pharmacy which will be expanded in a forthcoming edition.

At the undergraduate level, there are no courses in hospital pharmacy beyond that of an elective. Several colleges of pharmacy are beginning preliminary surveys to determine the demand for expanded programs in this field. At least one college now offers graduate work in hospital pharmacy and others are giving attention to this need. Facilities are also being developed to integrate academic training with hospital pharmacy experience, or internships, in affiliated hospitals.

ADR

DENTAL REMEDIES RECENTLY ACCEPTED BY A. D. A. COUNCIL ON DENTAL THERAPEUTICS

ANTISEPTICS AND ANTIBIOTICS[1]

Zephiran Chloride Solution 1:1,000: Zephiran chloride, 0.1 per cent; water, 99.9 per cent.

Zephiran Chloride Stainless Tincture 1:1,000: Zephiran chloride, 0.1 per cent; alcohol, 50 per cent; acetone, 10 per cent; water, 39.9 per cent.

Zephiran Chloride Tinted Tincture 1:1,000: Zephiran chloride, 0.1 per cent; alcohol, 50 per cent; acetone, 10 per cent; color and water, 39.9 per cent.

Zephiran Chloride Aqueous Solution 12.8%: Zephiran chloride, 12.8 per cent; water, 87.2 per cent. (This is a concentrated dosage form, intended for dilution with distilled water or other suitable solvent or mixture to produce the other accepted dosage forms of zephiran chloride. It is the most economical form in which to buy zephiran chloride if large quantities are to be used.)

Distributed by WINTHROP CHEMICAL CO., INC., New York.

Penicillin Troches, Abbott.—Each troche is stated to contain tragacanth, powder, 42.6 mg.; acacia, powder, 42.6 mg.; sodium carboxymethylcellulose, 19.0 mg.; sugar, powder, 745 mg.; penicillin calcium, 1000 units; flavor (creme de menthe), 0.66 mg.; magnesium stearate, 2.56 mg.

Indications: Penicillin troches are indicated as an adjunct in acute ulceromembranous gingivitis (Vincent's infection). They are contraindicated in cases demonstrating local sensitivity to the drug.

Local Effects, Systemic Toxicity and Actions: See "Penicillin," *Accepted Dental Remedies*, Ed. 12, p. 103.

Dosage: The dosage for penicillin troches according to Keefer et al. is as follows: Allow one troche to dissolve in the mouth. Repeat two or three times a day between meals.

Penicillin troches should be allowed to dissolve in the mouth as slowly as possible. This may be accomplished by placing them one at a time in the space between the cheek and the molar teeth, where they should be left undisturbed by the tongue.

In view of the fact that treatment of Vincent's infection with troches is in a somewhat experimental stage, a more intensive dosage might be desired. The most effective action will probably be obtained by keeping a troche in the mouth constantly during the waking hours, and placing one *in situ* just before going to sleep. The patient should be instructed that, if he awakens at night, he should place a fresh troche in his mouth before he goes to sleep.

Manufactured by ABBOTT LABORATORIES.

[1] *Accepted Dental Remedies*, Ed. 12, p. 72

NNR

PRODUCTS RECENTLY ACCEPTED BY THE A. M. A. COUNCIL ON PHARMACY AND CHEMISTRY

Council descriptions of drug products are published regularly in This Journal as they are accepted. Rules upon which the Council bases its action appeared in the July, 1946, issue (7:320, 1946) and may be secured in pamphlet form upon request to the Secretary, Council on Pharmacy and Chemistry, American Medical Association, 535 N. Dearborn St., Chicago.

SOLUTION OF EPINEPHRINE HYDROCHLORIDE (See New and Nonofficial Remedies, 1945, p. 292).

The following dosage form has been accepted:

BARRY BIOLOGICAL LABORATORY, DIVISION OF BARRY ALLERGY LABORATORIES, INC., DETROIT

Solution Epinephrine Hydrochloride 1:1000: 30-cc. vials. Each cubic centimeter contains epinephrine U. S. P. 1 mg. in isotonic solution of sodium chloride with chlorobutanol 0.5 per cent and sodium bisulfite 0.1 per cent as preservatives.

SULFATHIAZOLE (See New and Nonofficial Remedies, 1945, p. 202).

The following additional dosage form has been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Sterile Sulfathiazole: 5.0-Gm. sterilopes.

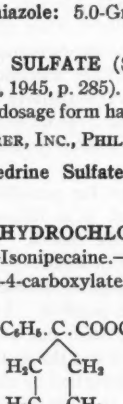
EPHEDRINE SULFATE (See New and Nonofficial Remedies, 1945, p. 285).

The following dosage form has been accepted:

WILLIAM H. RORER, INC., PHILADELPHIA

Solution Ephedrine Sulfate: 50 mg. in 1 cc. ampuls.

DEMEROL HYDROCHLORIDE.—Meperidine hydrochloride.—Isonipecaine.—Ethyl-1-methyl-4-phenylpiperidine-4-carboxylate hydrochloride.—M. W. 283.79.



The base ethylmethylphenylpiperidine carboxylate may be obtained by combining dichlorodiethylmethylamine with benzylcyanide and subsequent esterification; this is converted to the hydrochloride.

Actions and Uses.—Demerol hydrochloride possesses a minor atropine effect and predominant morphine-like analgesic properties. It is capable of depressing the cardiac vagus of the anesthetized animal to the point where faradic stimulation fails to elicit any cardiac effect. Such responses are reversible.

The spasmolytic action of Demerol hydrochloride is due in part to depression of the parasympathetic endings but is primarily the result of a direct papaverine-like depression of the muscle fiber.

Therapeutic doses produce a slight sedative and a decided analgesic action. Unlike morphine, Demerol hydrochloride is not a potent hypnotic. In man the analgesic effect of Demerol hydrochloride appears to lie between that of morphine and codeine and persists for from five to six hours.

Although it has not been possible to demonstrate the development of physiologic dependence to Demerol in animals, the drug does possess a moderate degree of addiction liability. The development of tolerance to the drug has been demonstrated in man, and it has been shown that Demerol may be substituted for morphine in addicted individuals with prevention of the morphine withdrawal syndrome. Furthermore, mild withdrawal symptoms have been observed in susceptible individuals purposely addicted to the drug.

The possibility of development of psychic dependence to Demerol must also be kept in mind, since the drug will produce a euphoria in some individuals which lasts for an hour or more, depending on the dose.

Demerol hydrochloride is indicated for the alleviation of pain, particularly pain of spastic origin, and in the majority of conditions in which morphine or other opium alkaloids are generally employed. In obstetrics it may be used to lessen the severity of labor pains and, in conjunction with barbiturates, to produce obstetric amnesia.

Dosage.—For most medical and surgical conditions the average adult dose of Demerol hydrochloride is 0.1 Gm., administered either intramuscularly or orally. In some patients pain is controlled by as little as 50 mg. Others suffering from severe pain require 0.15 Gm. For the production of analgesia in obstetrics, 0.1 Gm. is given intramuscularly as soon as contractions occur at regular intervals. If labor is rapid or if the cervix is thin and dilated (2 to 3 cm. or more) the second dose may be given as soon as one-half hour after the first one. A third dose may be necessary an hour or two later, depending on progress.

If the production of amnesia is desired, one of the barbiturates may be given when the cervix is dilated 4 or 5 cm. or when the third dose of Demerol hydrochloride is administered. In the majority of cases this procedure will insure adequate amnesia for from four to six hours. When barbiturates are used with Demerol hydrochloride for this purpose they are effective in considerably smaller doses than when used alone.

Tests and Standards.—

Demerol hydrochloride occurs as a fine, white crystalline, odorless powder; stable in the air at ordinary temperature;

soluble in water, acetone and ethyl acetate; slightly soluble in ethanol and isopropanol; insoluble in benzene and ether. Its aqueous solution (1 in 10) is acid to litmus. Demerol hydrochloride melts at 186 to 189° C. Aqueous alkali carbonates and hydroxides precipitate the free base as a water-white to a pale yellowish solid.

For tests and standards see *J. Am. Med. Assoc.*, 132:147 (1946).

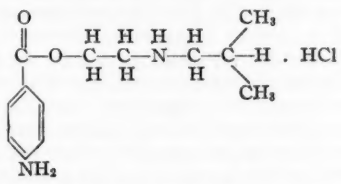
WINTHROP CHEMICAL CO., INC., NEW YORK

Solution Demerol Hydrochloride, 50 mg. per cc.: 2-cc. ampuls.

Tablets Demerol Hydrochloride: 50 mg.

U. S. patent 2,167,351 (July 25, 1939; expires 1956). U. S. trademark 281,130.

MONOCAINE HYDROCHLORIDE.—2 - Isobutylaminoethyl *p*-aminobenzoate hydrochloride.—2-*p*-Aminobenzoxy- N - isobutyl - ethylamine hydrochloride.—The hydrochloride of the ester formed from *p*-aminobenzoic acid and N-isobutyl ethanolamine.—$C_{13}H_{21}ClN_2O_2$.—M. W. 272.78.



Actions and Uses.—Monocaine hydrochloride is a local anesthetic similar to procaine hydrochloride. It is used for nerve block anesthesia in dentistry or other surgical operations. Present evidence does not warrant recommendation for its use for topical or surface anesthesia of mucous or other membranes. Its effects, either with or without the addition of epinephrine hydrochloride, are qualitatively identical in every respect with those of procaine. Quantitatively, monocaine has been shown to have about one-third more anesthetic and toxic potency than procaine (i. e., monocaine solutions of three-fourths the concentration of procaine solutions are approximately equivalent).

Dosage.—For dental or other minor surgery, a 1 per cent solution with epinephrine 1:75,000 may be injected to obtain nerve block anesthesia. In major surgery or other procedures requiring nerve block anesthesia equivalent to that produced by 2 per cent procaine, a 1.5 per cent solution of monocaine with epinephrine 1:100,000 may be used. (See caution under the general article Local Anesthetics.)

Tests and Standards.—

Monocaine hydrochloride occurs as a white, odorless, crystalline powder possessing a bitter taste and anesthetizing effects. It melts within the range 192–196° C. It is sparingly soluble in water, slightly soluble in alcohol and chloroform, very slightly soluble in benzene and practically insoluble in ether. The *p*H of a 1 per cent aqueous solution is about 4.7.

For tests and standards see *J. Am. Med. Assoc.*, 132:147 (1946).

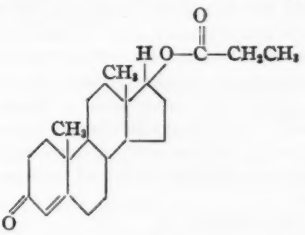
NOVOCOL CHEMICAL MFG. CO., INC., BROOKLYN

Monocaine Hydrochloride Solution 1% with Epinephrine 1:75,000: 1-cc., 2-cc., 3-cc. and 5-cc. ampuls; 1-cc., 2-cc., 2.5-cc. and 5-cc. Anestubes (syringe cartridge); 2½-cc. and 5-cc. Novampuls (ampul type syringe); and 30-cc., 60-cc. and 120-cc. bottles. Each cubic centimeter contains monocaine hydrochloride 10 mg., epinephrine U. S. P. 0.013 mg., sodium bisulfite 2.0 mg. and sodium chloride 6.5 mg. in sterile distilled water.

Monocaine Hydrochloride Solution 1½% with Epinephrine 1:100,000: 1-cc., 2-cc., 3-cc. and 5-cc. ampuls; 1-cc., 2-cc., 2½-cc. and 5-cc. Anestubes (syringe cartridge); 2½-cc. and 5-cc. Novampuls (ampul type syringe); and 30-cc., 60-cc. and 120-cc. bottles. Each cubic centimeter contains monocaine hydrochloride 15 mg., epinephrine U. S. P. 0.01 mg., sodium bisulfite 2.0 mg. and sodium chloride 4.5 mg. in sterile distilled water.

U. S. patent 2,139,818 (Dec. 13, 1938; expires 1955). U. S. trademark 353,653.

TESTOSTERONE PROPIONATE.—The propionic acid ester of testosterone.—Δ4-androsten-17(α)-propionate-3-one.—$C_{22}H_{32}O_3$.—M. W. 344.48.—Testosterone propionate possesses androgenic properties. It may be prepared synthetically from cholesterol as the starting material or from testosterone isolated from bull testes. The structural formula of testosterone propionate may be represented as follows:



Actions and Uses.—Testosterone propionate is primarily useful to supply testicular hormone for the treatment of deficiency or absence of this internal secretion of the male. It may therefore be of value in the treatment of prepuberal and postpuberal eunuchoidism or hypogonadism (deficiency states) and in postcastration and eunuchism (absence of testicles). In the latter instances treatment must be regarded as replacement therapy and is of benefit only as long as it is continued.

Its use in eunuchoidism is intended to promote prepuberal development of primary and secondary sexual characteristics or to relieve postpuberal constitutional symptoms attributable to deficient secretion. In the treatment of constitutional symptoms in young males it should be borne in mind that less is usually needed to obtain relief than the amount required to promote pubescence and development of infantile genitalia, and that it is unwise to stimulate full sexual maturity in youths who are psychologically and otherwise physically unprepared for adult life. In eunuchoidism not due to primary testicular hypoplasia, efforts to eliminate secondary etiologic factors should take precedence over the use of androgens.

In adults, hypogonadism (functional deficiency) manifested by constitutional symptoms and effemi-

nacy without striking anatomic changes, symptomatic improvement may follow androgenic therapy. Atrophy of accessory male structures that follows castration or is associated with eunuchism may also be effectively prevented or these organs restored to normal and maintained by continuous therapy.

The use of androgens in the treatment of other conditions such as cryptorchism, the "male climacteric," angina pectoris, ovarian dysfunction (functional uterine bleeding), dysmenorrhea and other gynecologic conditions is experimental and cannot be recognized until more conclusive evidence becomes available.

Dosage.—Testosterone propionate is administered intramuscularly in doses ranging from 5 to 50 mg. from two to six times weekly, depending on the response obtained. To induce pubescence in eunuchoidism, 10 mg., increased as indicated to 25 mg. three times weekly, may be employed over a period of several weeks. To relieve constitutional symptoms as little as 5 mg. at similar intervals may be sufficient. Depending on the condition and the effect desired, the maintainence dose must be determined in each individual case. Priapism is indicative of excessive dosage, and its production is an indication for temporary withdrawal of the drug. Caution is also necessary to avoid precocious sexual development in young boys. Its indiscriminate use should be guarded against, since the drug may produce irreversible masculinizing phenomena in the female. Testosterone propionate has a standard potency of 50 international capon units per milligram and is usually dissolved in oil for intramuscular injection.

Tests and Standards.—

Testosterone propionate occurs as an odorless, white to pale yellow, crystalline powder. It is insoluble in water but soluble in organic solvents such as alcohol, chloroform and ether; it may be dissolved in vegetable oils. Testosterone propionate melts between 118 and 122° C.

For tests and standards see *Jour. Am. Med. Assoc.*, 132: 213 (1946).

RARE CHEMICALS, INC., HARRISON, N. J.

Testosterone Propionate in Oil: 1-cc. ampuls of 5 mg. per cubic centimeter, 10 mg. per cubic centimeter and 25 mg. per cubic centimeter, equivalent to 250, 500 and 1250 international capon units per cubic centimeter, respectively, in sesame oil.

CABASIL: QUACKERY UNLIMITED

(*Based on a Report of the Council*)

The proprietary, Cabasil (Cabasil, Inc., 800 Bankers Security Bldg., Philadelphia), has been marketed in a variety of dosage forms: oral, enema, rectal ointment, suppository (rectal and vaginal) powder, nose and throat powder, surgical powder, concentrate fluid, implants ("seeds"), ointment (mild), concentrate ointment (strong), foot powder and special forms such as capsules for prevention of water-borne infection.

It is not known whether all forms have the same composition, but in 1945 the laboratory of the American Medical Association reported that a sample of Cabasil powder consisted "essentially of a mixture of magnesium oxide, magnesium hydroxide and barium sulfate, together with a small amount of organic substances such as iodoform."

The sources of distribution of Cabasil appear to stem primarily from the promotional interest of Dr. Stuart Kabnick, a practicing dentist of 326 S. 21st St., Philadelphia, whose previous activities have also been the subject of critical comment by the Council on Pharmacy and Chemistry. Early in the war letters to one organization from Dr. Kabnick bore the address 21st and Delancey Sts., Philadelphia, the same as that attributed to the "Pennsylvania Institute of Chemurgic Therapology," used as a caption for a mimeographed leaflet promoting Cabasil and its claimed mode of action in inflammatory processes. Apparently this institution serves as an advertising outlet for the "research" activities of Dr. Kabnick.

During the war Dr. Kabnick made some effort to interest a research organization engaged in war work in Cabasil, principally for use by the armed forces in the treatment of battle casualties, but he refused to reveal the composition. Because of considerable political pressure, the research organization asked a group of consultants to review the claims made by Dr. Kabnick for use of the preparation in wounds and burns. After a preliminary investigation this group concluded that the claims were supported only with inaccurate testimonials and that there was no warrant for further investigation of this proprietary remedy to have it recommended to the armed forces.

A mimeographed leaflet on the so-called advantages of the use of Cabasil technique consists of a list of amazing claims for the efficacy and economy of "implants" and "powder" in the treatment of the soldier with infected battle wounds, including osteomyelitis and gangrene, without the use of instrumentation or surgery. One version of the leaflet states that "one Cabasil plant into his bullet wound or wounds immediately after he is wounded, he will require little or no further attention." "The bleeding will be stayed and there will be little or no infection. Most bullet wounds heal with one plant."

Another promotional brochure outlining the forms and indications of Cabasil lists over thirty unrelated conditions, including such diseases as allergy, arthritis, Buerger's disease, colds, colitis, chancroid, dysentery, gangrene, gastroenteritis, osteomyelitis, pneumonia and trichinosis. There are no published reports to substantiate any of the claims made.

The Council condemns the manner in which Cabasil has been exploited to the medical profession and public. In view of Dr. Kabnick's past record in promoting a variety of proprietaries, the Council warns against the possibility that the promoter may proceed along another tangent by adoption of a different name and set of conditions on which to base criteria for his so-called "ideal" disinfectant.

—*J. Am. Med. Assoc.*, 132: 144, 1946

Typical Days

FROM THE SECRETARY'S SEPTEMBER DIARY

—1st—

AFTER completing the story of the Pittsburgh Convention for the JOURNAL with Glenn Sonnedecker, returned by auto over the Pennsylvania Turnpike to Washington in a seven-hour drive broken only by a stop for dinner. A beautiful day, with few on the road and plenty of time to reflect on the events of the previous week.

—2nd—

Labor Day, a holiday, and therefore a good day to be at the desk, for telephone interruptions are few. Glad to welcome Charles H. Evans who dropped by for a chat on the future professional relations program which should get off to a good start after the interest shown at Pittsburgh. Later to Alexandria for a good dinner at the famous "Inn."

—3rd—

Everyone back on the job after the long week-end holiday and ready to pick up where we left off before the convention. New officers, new committees, new thoughts and new suggestions are stimulating to the Headquarters staff and there is plenty of activity to look forward to. During the morning a visit from Mr. and Mrs. Charles Evans on their way back to Georgia. It was a pleasure to show Mrs. Evans, new president of the Women's Auxiliary, the nicely furnished lounge for our women employees. We are very grateful to the Auxiliary for having taken on the financial responsibility for furnishing these quarters. And now in the middle of the afternoon, leaving for Red Bank for a few days of rest after the strenuous convention days, and it was a delightful ride via Belair, Md., where we looked in on Lloyd Richardson. Stopping at Camden, N. J., for dinner, met Dr. Charles E. Vanderkleed, distinguished pharmaceutical chemist who taught us most of what we know about drug control.

—5th—

Today a pleasant automobile trip to Easton where the Mack Printing Co. produces our journals. Quite a reunion to meet so many co-workers of years ago when we labored on the *News Edition* of *Industrial and Engineering Chemistry* and all looking well with few signs of the passage of time. With Sonnedecker finishing the proof reading and approval of the final pages of the convention report and then returning to Red Bank by way of Trenton, dropping Sonnedecker off for the return to Washington by train.

—10th—

Today a session with the architects about the memorial flagstaff which Dr. Dunning has generously provided for. And it will be a beautiful addition to the Headquarters Building which has seemed isolated on parade days and holidays with no flag unfolding to the breeze.

—12th—

And now a meeting with the Proprietary Association's Secretary Barta and Editor Swain—a subcommittee of the National Drug Trade Conference Committee on Uniform State Pharmacy Laws. It is hoped that some way can be found to avoid the antagonisms of various divisions of the drug industry before committees of the state legislatures when amendments to pharmacy laws are considered which involve regulation of the sale of drugs and medicines. Proprietary medicine manufacturers have for years opposed restrictions of the sale of their products to pharmacies. This is the bone of contention and compromise seems far off at times. Later in the day meeting with the Steering Committee on the Pharmacy Corps legislation where strategy for the expected fight against abolition of the Pharmacy Corps was developed.

—13th—

Among the callers today gladly welcomed Richard Deno who was on a visit to some of pharmacy's nearby historic shrines. He is President of "Friends of Historical Pharmacy" and always a welcome visitor. At the desk until midnight cleaning off accumulated routine matters.

—16th—

On an early train from Red Bank to New York and then catching the 10 o'clock train for Boston, after telephone conversation with Elmer Bobst who is active in the American Cancer Society and will help materially to work out Pharmacy Week observance which is to be dedicated to the cancer control program in 1947. Arriving in Boston at 1:50 p. m.,

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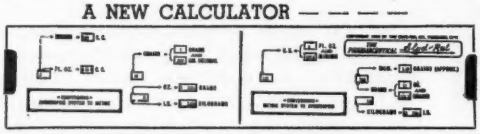

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transferred immediately to the North Station for the afternoon train to Portsmouth, N. H., where the New Hampshire Pharmaceutical Association is in annual convention assembled. Waiting at the station in Portsmouth were Messrs. Callaghan and Smith who whisked us away to the Wentworth Hotel where a comfortable room and all the courtesies of a good hostelry and good hosts were in evidence. And now changing rapidly into "black tie and tux" joined the New Hampshire pharmacists at their annual banquet graced by Governor and Mrs. Dale among other distinguished guests. The honorary membership award this year went to Dean Kendig and we told of the things that lie ahead for the pharmacists of the nation, with George Moulton doing honors as Master of Ceremonies and he always does this well. It was a pleasure to renew friendships with many New Hampshire and Greater New England friends who visit these conventions regularly.

—17th—

After an early breakfast with W. Paul Briggs and Dean and Mrs. Kendig at the same round table, leaving on the morning train for Boston and lucky to get a seat on the noon train for New York which rolled into Grand Central Station on time at 4:35 p. m. After contact with the Washington office by telephone and dinner at the Chemists' Club, to Red Bank for the night.

—18th—

On the early morning train from Red Bank to New York for a conference with John Price Jones and his associates on the Pharmacy Week program as related to the American Cancer Society's public relations activity and then to Washington, arriving in the middle of the afternoon in time to complete the most pressing "new business."

—19th—

Today a session with representatives of the Fine Arts Commission which is charged with approval of all new building construction, including our memorial flagstaff. At night with Justin Powers and George Beal for dinner at the Statler and later to the office to burn a little midnight oil in an effort to reduce the "unfinished business." The inanimate dictaphone is a great help in this procedure.

—20th—

A profitable lunch hour spent with Justin Powers in discussing publication matters. Later answering questions propounded by the Director of the Pharmaceutical Survey and then a meeting, in our beautiful reading room, of the Executive Committee of the American Social Hygiene Association whose members were inspired and pleased by what they saw of our building and facilities. To dinner at the Statler with the Board of Directors of the A. S. H. A., followed by a spirited and fruitful meeting at which major policies were discussed and determined.

—21st—

All this Saturday working with first one and then another member of the staff who required decisions on this and that including some re-arrangement of offices to provide for new personnel, some re-assignment of duties to take full advantage of the specialized training of those recently added to the staff; also a bit of shopping.

—23rd—24th—25th—

After the week-end at Red Bank, to Atlantic City for the annual convention of the National Wholesale Druggists' Association. A fine turn-out of the drug industry and an excellent program which included such headliners as Elliott, Fishbein, Swain, Weicker, Nolen, Newcomb, and others. Also luncheons and dinner parties galore, and of course "cocktail hours," provided by generous hosts among the manufacturing and wholesale fraternity. Back to Washington on the 25th.

—26th—

On the 7 a. m. train for Philadelphia to meet George Beal for a visit to Sharp and Dohme Laboratories at 11 a. m. Most interesting conversation with President John Zinsser on international health affairs and on the work of the A. Ph. A. Laboratory. After luncheon at the Bellevue-Stratford met Robert Lincoln McNeill, President of McNeill Laboratories

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at the Union League where there was much conversation on the future of A. Ph. A. affairs with special reference to the influence of the Laboratory on the formulation of adequate standards for drugs.

—28th—

Glad to have an opportunity to discuss pharmaceutical affairs in South America with Dr. Goetz who came to confer a "corresponding membership" in the Argentine Pharmaceutical Society upon the Secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION and present a diploma and gold medal in honor of the occasion. This expression of friendship and good will was gratefully accepted on behalf of American pharmacy.

—30th—

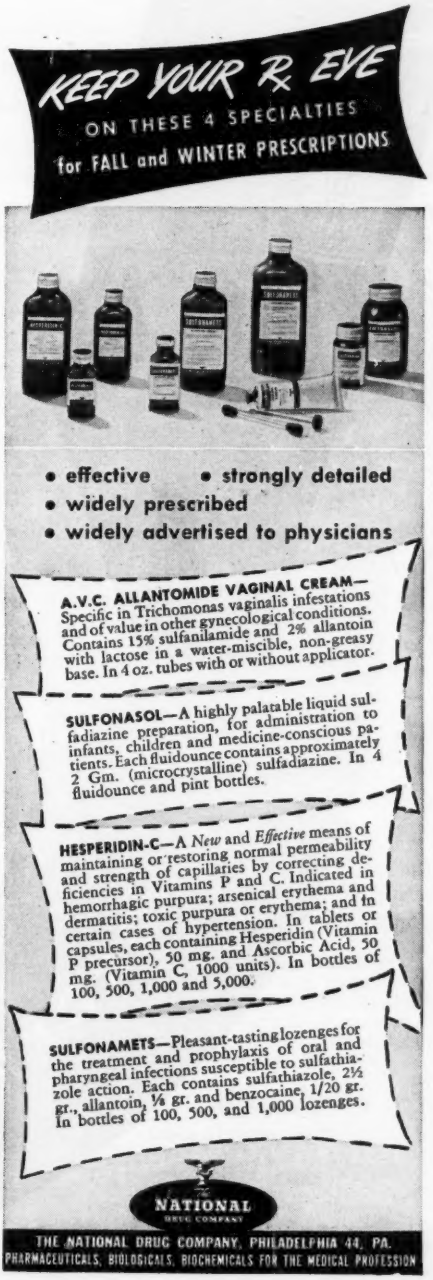
A brief visit to the scientific and commercial exhibits of the D. C. Medical Society at the Statler, meeting many medicos of prominence including Drs. L. L. Williams and H. VanZyle Hyde of the U. S. Public Health Service. In the afternoon a visit from Mr. Caemerer, Secretary of the Fine Arts Commission, who inspected the building and especially the site for the memorial flagstaff. And so another month completed.

DUNNING PRESENTS PAINTING TO MARK ETHER CENTENNIAL

A feature of the one-hundredth anniversary of the first administration of anesthetic ether, which was celebrated with appropriate ceremonies at the University of Maryland School of Medicine, was the presentation of a painting entitled "The First Administration of Anesthetic Ether" to the Department of Pharmacology by Dr. H. A. B. Dunning, chairman of the Board of Hynson, Westcott and Dunning of Baltimore, Md., former president of the AMERICAN PHARMACEUTICAL ASSOCIATION and now a member of its Council.

Ceremonies incident to this occasion included an address on "Surgery Before Anesthesia" by Dr. Henry E. Sigerist, professor of the history of medicine, Johns Hopkins University; an address on "Dr. W. T. G. Morton and Ether" by Dr. J. Ben Robinson, dean of the School of Dentistry, University of Maryland; and an address "Anesthesia Today and Tomorrow" by Dr. Henry S. Ruth, editor, *Anesthesiology*.

The painting donated by Dr. Dunning was based upon a daguerreotype and was done by Stanley M. Bell. It was unveiled by Constance Black, an anesthetist who has voluntarily subjected herself to the action of several new anesthetics in connection with researches on newer anesthetic agents under the direction of John C. Krantz, Jr. Dr. Krantz, professor of pharmacology in the School of Medicine, presided at the ceremony.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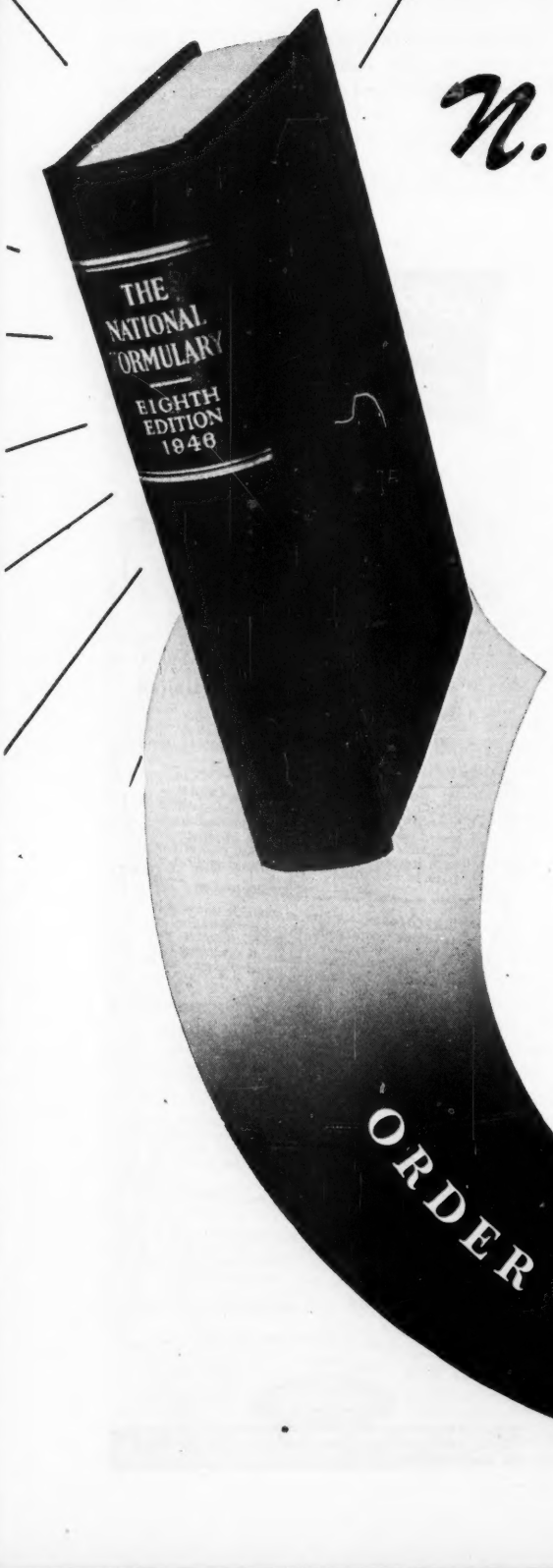

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Henderson, Jean, Washington
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Crump, John D., Macon
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Maher, Frank T., Oak Park
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Karbal, William H., Detroit
Koprince, Daniel, Detroit
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Robson, James R., Allegan
Rykert, Glenn E., Detroit
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Wolf, Richard, Grand Rapids
Wood, Thomas, Detroit

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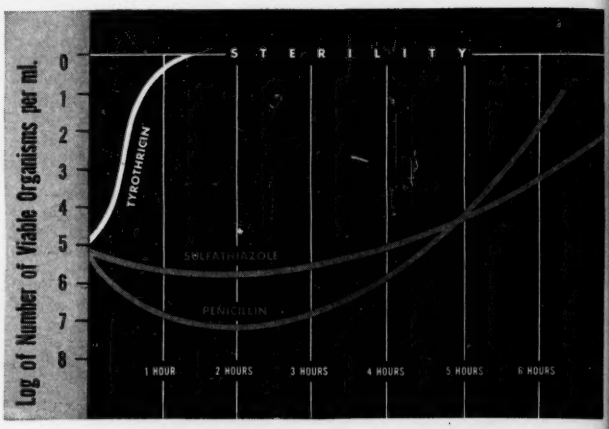

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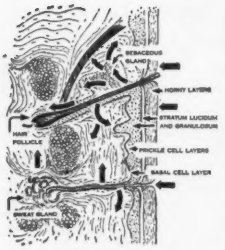

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